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THE DIAGNOSIS OF GASTRIC ULCER AS TESTED BY OPERATION.

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I report herewith a study of fifty consecutive cases of gastric, pyloric, and duodenal ulcer, in which the diagnosis was placed beyond all doubt by the findings at operation. I might have collected many more personal cases, had I included the much larger number not coming to operation in which the diagnosis was still reasonably clear, but this would have introducted doubt as to the real condition. A number of hospital cases, which were equally well verified by autopsy, are omitted for lack of sufficiently clear histories. My records are less complete than they should be, but many of the cases were seen but once or twice before operation. The patients were all operated upon by nine of our Colorado surgeons.

Twenty-eight of the patients were males, twenty-two females. There were twenty-one in the fourth decade, twelve in the third, nine in the fifth, six in the sixth, and two in the second. Twenty-eight of the ulcers were active at the time of operation; twenty-two were healed, but had led to symptoms demanding operation because of contraction of the cicatrix, formation of adhesions, etc.

In eleven cases there had been trouble for from eighteen to thirty years. In five of the cases the ulcers were still active. Nine had existed ten to fifteen years, five for five to ten years, seven for three

to five years, eight for two years, and ten for one year or less. Thirty-three of the ulcers were (or had been) pyloric, thirteen were definitely gastric, and four definitely duodenal. Case sixteen had a scar of a healed ulcer in the pylorus and an active ulcer two inches above. Case twenty-six had an old scar at the pylorus and a similar one below it. Of the thirty-three pyloric ulcers, eighteen were still active.

In thirty instances the stomach was dilated, fourteen being from active ulcers and sixteen from scars of healed ulcers. In many of the cases adhesions were in part responsible for the obstruction. In but one of the four definitely duodenal cases was dilatation noted. In twenty-six of these dilated stomachs splashing was noted.

I have studied these cases expressly to bring out the relative frequency and value of the different symptoms and signs of ulcer, for I believe the diagnosis is not made in many cases justifying it, much to the detriment of the patient.

Of the fifty cases, thirty-three had had vomiting (66 per cent.); seventeen had not. Seventeen had had hematemesis (34 per cent.) and four had passed blood by the bowel (8 per cent.). Forty had had sour stomach to a notable degree (80 per cent.). Forty-one had had notable pain (82 per cent.), and, when examined, thirty-five (70 per cent.) had tenderness, and thirty (60 per cent.) muscular rigidity in the region of the stomach. Thirty-seven (74 per cent.) had lost from ten to fifty-five pounds in weight.

Records of the chemical analysis of the stomach contents are available in but thirty-six of the cases. Several demanded instant operation, others were seen but once in consultation, and in others, various reasons prevented a full and careful investigation such as should be made in this important class of cases. Of the sixteen cases of active gastric and pyloric ulcer examined, twelve had high acidity, four were below normal. Seventeen of the cases in which we found a healed ulcer were examined chemically, and fifteen were below normal in acidity. In case fifteen, with hyperacidity, the healed ulcer was apparently of no moment, and the real cause of the obstruction was a Treitz's hernia, the duodenum being completely blocked, as it had doubtless been many times before, in the opinion of Dr. Freeman and myself. In only two cases of duodenal ulcer was gastric analysis available; a low acidity existed in one of these, hyperacidity in the other. Several of the cases found by me to have a low acidity had previously had hyperacidity.

In many cases tenderness over the lower ribs, generally on the left, was noted, and in others great hyperesthesia over the immediate seat of the ulcer. Rigidity is present in so many cases that we must account for it otherwise than as the result of an active ulcer. The adhesions seen so generally about a healed ulcer are, I believe, a sufficient explanation.

Case eighteen had the scar of an old ulcer adherent to the liver; case thirty-eight a scar adherent to the pancreas, and cases four, thirty-two and forty-five, scars adherent to the gall-bladder. Case nineteen had an hour-glass stomach from distortion produced by the healing of a large ulcer. Case forty-five showed a chronic pancreatitis. Cases six, eight, and eleven were operated on for perforation of a gastric ulcer, and nine for an incomplete perforation near the pylorus, lymph flakes being found upon the peritoneum over the ulcer, with delicate adhesions to the adjacent loop of bowel. In case six the perforation was a large one on the greater curvature, and was seen nearly twenty-four hours after the accident. This was the only fatal case of these four. They were operated upon by Drs. Bagot, Fleming, Freeman, and Perkins.

All but the fatal case (six) just mentioned, and case thirty-two, in which old adhesions to the gall-bladder were broken up, but no dilatation existed, and case forty-eight, were treated by gastro-enterostomy—several times with an additional operation upon the gall-bladder or appendix—except that in two of the cases, Finney's operation was preferred. Case forty-eight had a large cancer developed upon the base of the ulcer. She had about a third of the normal acidity in the stomach contents; an exploration only was made.

There were six fatalities. Case four died of shock following a gastro-enterostomy, in which, owing to old and extensive adhesions, the clamp could not be used; the operation was, therefore, much prolonged, and more blood than usual was lost. Case six failed to recover from the repair of a twenty-four-hour-old perforation. Case thirteen died from shock following a secondary operation for the incarceration of small intestine in a Treitz's hernia, after a gastro-enterostomy had been successfully carried out. Case fourteen died from acid intoxication following the anesthetic. Case twenty-seven, with a greatly dilated stomach from the scar of an old ulcer in the pylorus, was sent to his home eighty miles away, because of chronic lung trouble with myriads of pneumococci in the sputum, which we thought forbade operation, and especially an anesthetic. He came back in a fortnight and said that he preferred the chance of death from pneumonia to his present condition. He died in forty hours from a very virulent, acute pneumonia as we had feared. In case forty-two the duodenum was obstructed by the pressure of the superior mesenteric vessels after the operation, and death occurred from this and from hemorrhage into the stomach.

Of the remaining forty-four cases, thirty-two may be classed as cured, ten as more or less relieved, while one, with a dilated, atonic stomach, is, if anything, worse off than before, and the case with cancer remains as before so far as the operation is concerned.

We have found, as the Mayos have noted, that those patients with the stomach dilated beyond all hope of regaining its motor

power generally fail to improve. Several instances have been observed by those of us interested in this series of cases, in which a simple atonic dilatation was associated with pronounced neurasthenia, and none has been materially improved by operation.

Cases thirty-eight and thirty-nine were brothers, and another brother is reported to have died of perforation of a gastric ulcer. Cases twenty-one and twenty-nine were sisters, both trained nurses, and neither was aware of anything more than a slight indigestion, yet both had healed ulcers blocking the pylorus. Several of the cases of pyloric ulcer had previously been operated upon for supposed gallstones or appendicitis, with negative findings. I think this history is much more common in duodenal than in gastric ulcer.

The idea is widespread that dilatation of the stomach occurs in ulcer only as the direct result of mechanical obstruction. There can be no question that in many cases, in which at operation the pylorus admits a finger freely, there is nevertheless great dilatation of the stomach. The influence of spasm of the pylorus from the irritation of an ulcer in that region, possibly from hyperacidity alone, in the causation of such a dilatation is most important. I believe that surgical intervention is indicated in practically all of these cases, for if the ulcer heals a later dilatation of the stomach, from a contracting scar, will probably call for the surgeon's aid. If they must be operated upon, the earlier the better.

It will be noted that pain, persistent sour stomach, tenderness, vomiting, and rigidity were the most frequent indications of ulcer, occurring respectively in 82, 80, 70, 66, and 60 per cent. of the cases reported. Gastric hemorrhage occurred in but 34 per cent., and bloody stools in but 8 per cent. Curiously no one of the four definitely duodenal ulcers gave a history of hemorrhage of any kind.[1]

In case forty the patient came to me for hiccough coming on at intervals over a period of eleven years, and existing for a week or two at a time with great severity. I found a history of hematemesis, vomiting, and sour stomach, with pain, tenderness, rigidity, and high gastric acidity. I recommended gastro-enterostomy for the supposed ulcer as a cure for this hiccough, which was alarming at times. Dr. I. B. Perkins operated upon him with complete success, the stomach symptoms and the hiccough remaining absent to the present writing—eleven months after operation. The lesion was a saddle ulcer near the pylorus.

In one of these cases, and one other recently seen, a small hernia was present in or near the linea alba, and contributed much toward the discomfort complained of. In each case acute pain was caused by pressure upon it, and complete relief was obtained by operation

[1] Since closing this series of cases, I have seen one such case fatal from repeated hemorrhages after gastro-enterostomy was done.

directed toward cure of the hernia and the simultaneous correction of the pyloric obstruction in the one already operated upon.

The frequent finding at operation of enlarged lymph nodes should be noted as well as the chance of error in basing a diagnosis of cancer upon their presence, with an associated thickening about the pylorus. I have seen a tumor at the pylorus the size of an egg disappear with the healing of an ulcer in this region.

I find myself frequently unable to distinguish between pyloric and doudenal ulcers, while those situated above the outlet may generally be diagnosticated as being so placed from the absence of obstructive symptoms, and frequently from local, acute tenderness to the left of the pylorus. The tenderness is certainly more marked in ulcers on the anterior surface of the stomach than elsewhere, in my experience. I agree with Graham's statement, that pain is relieved for a longer time after eating in doudenal and pyloric ulcers than in those above the pylorus.

In these fifty cases there were but two errors in diagnosis, excepting as to the exact location of the ulcer, a point of minor importance. In case thirteen, owing to persistent sour stomach for a whole summer ten years ago, with acute symptoms and high acidity of recent origin, I diagnosticated an old healed ulcer with a recent acute one, or else an active one which had never entirely healed in all this time. We found a scar of a healed ulcer two inches long on the greater curvature, and Treitz's hernia already mentioned, which accounted for the acute symptoms.

In another case my diagnosis was very positively in favor of cystic gallstones, but it proved to be duodenal ulcer. With the same symptoms and absence of hemorrhage, I fear I should repeat the mistake in a similar case. No permission to give a test meal could be obtained in this instance. I have made the same or a reversed error before. I should state, however, that seven or eight of my patients were operated upon while I was collecting this series, in which, from its known frequency as a cause, scar of a healed gastric ulcer was erroneously diagnosticated as the origin of a dilated stomach, when this was really purely atonic or due to adhesions from old gall-bladder disease, spasm from irritation of a concretion in the appendix, kink from a floating right kidney, from a prolapsed colon dragging on the stomach, or other near-by disease.

If I were entitled to make any criticism upon our usual attitude toward the diagnosis of gastric ulcer, I should say that we are, first, inclined to look upon the disease as a comparatively rare one instead of a very common one; second, that we are inclined to look for a too classical history, especially of vomiting and hematemesis, with a high acidity reported from the laboratory; third, we are inclined to place altogether too much reliance upon the chemical findings and too little upon the results of the physical examination, and are therefore making far too many diagnoses of hyperacidity when the finding

by careful examination of the slightest unilateral rigidity in the epigastric region, associated with local tenderness, should lead us to diagnosticate ulcer instead.

The chemical evidence is so extremely variable, that we should not let it overweigh the more reliable findings of the bedside examination. After a chronic gastritis is set up, or a marked dilatation from obstruction occurs, or the patient becomes anemic, the hyperchlorhydria often disappears, and its absence should not count against the diagnosis of ulcer. Rather than to look too narrowly for exactly this or that evidence, we should take the broader ground that ulcer probably exists in most patients complaining of persistent indigestion, even though not of an acid character, if pain, tenderness, vomiting, and rigidity, or two or three of these phenomena be present, and even though hyperacidity be not proved. Most of us incline to wait for too positive and classical a picture before making the diagnosis, as is so often the case with the diagnosis of pulmonary tuberculosis and other common diseases.

It will be noted that the errors mentioned have been rather on the side of diagnosticating ulcer when the dilated stomach, which really led to the diagnosis, was caused by some other condition. Yet no harm comes from this error since the dilatation often calls for operation, while a failure to diagnosticate ulcer, because, perhaps, the evidence is not conclusive, leaves the patient exposed to still further dilatation of the stomach, to hemorrhage or perforation, to neurasthenia from imperfect nutrition, and other ills that follow chronic ulcer. Our patients will be better off if we lean a little too much to the side of ulcer, and too little to that of simple hyperacidity.

I think there can be no question that ulcer of the stomach is much more frequent than we generally believe; that a scar may be frequently found blocking the pylorus in those in whom no symptoms have pointed toward ulcer, so far as an intelligent patient can inform us; that ulcer is probably present in the majority of cases of persistent sour stomach; that the finding of tenderness and rigidity over the stomach in the latter class of cases should be regarded as practically clinching the diagnosis, except in certain neurotic individuals; that a markedly dilated stomach in a young patient, not especially neurasthenic, should raise a presumption of pyloric ulcer or its results, if there have been any symptoms of indigestion in the past; that no neurasthenic should be treated without first investigating the size and digestive power of his stomach, regardless of the presence or absence of a history of ulcer; that patients not helped promptly by medical treatment should be studied carefully from a surgical standpoint; that the bedside examination must be given much greater weight in the diagnosis than the report from the laboratory; and that the diagnosis of ulcer may be made with very reasonable certainty if a careful investigation be carried out.

THE DIET IN TYPHOID FEVER.[1]

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In the absence of specific therapy, the importance of diet cannot be overestimated. This fact was keenly appreciated by the old masters in medicine: a casual historical retrospect shows the fever-besieged patient stimulated to the utmost with medicine and food, or subjected to the mercies of depleting drugs, venesection, and starvation, according to the prevailing dicta of the day. As physicians began to classify diseases, treatment, including diet, became more rational; but until the laboratories contributed their share to our knowledge of the functions of the body in health and disease, dietary rules were mainly empiric. Graves "fed fevers" because he saw excellent results from feeding. At present the clinician is influenced by the knowledge which results from scientific activity in the laboratories; he not only knows the exact anatomical changes produced by the disease he is treating, but he also has at his command an ever-increasing fund of facts relating to disturbances of function or to the complex problems of the chemistry of the body. Normal metabolism is in general understood, and much light has been thrown on the more difficult question of metabolism in disease. The conclusions from laboratory experiments are made doubly valuable or are nullified for practical purposes by a careful application of results at the bedside, and the spirit of modern medicine demands such a correlation.

This relation between the laboratory and the ward—the science and the art—has been especially prominent in the more recent studies on typhoid fever. In this paper I shall bear this point of view in mind as I briefly review the underlying principles of nutrition in typhoid fever, the conclusions drawn from the application of these principles to experimental studies, and finally the results of testing these conclusions at the bedside.

Various as are the manifestations of typhoid fever, there is yet one feature common to all cases: the course of the illness is a long-drawn-out battle between the patient and the disease. Since in all battles the strength of the combatants is to be preserved, this rule of more actual warfare is adopted in medicine to the conflict with such diseases as tuberculosis and septicemia. Starvation is in itself a disease with various symptoms due to disturbed metabolic processes, and if Ewing's[2] work is correct most of the symptoms of

[1] Read at the Semi-annual Meeting of the Southwest Virginia Medical Society, Bristol, Virginia, December 3 and 4, 1908.

[2] Nitrogen metabolism in Typhoid Fever. Med. Record, March 30, 1907, p. 537.

typhoid fever are caused by somewhat similar metabolic changes. Leaving for later consideration certain specific theoretical and practical objections to this statement and accepting as true the broad comparison, it becomes evident that in typhoid fever our therapeutic goal should be the strengthening of our patient to the full limit of good, without harming him. Food at once must be considered the main weapon in our hands, and we should provide a diet with sufficient nutrition while we remember the handicaps under which the patient fights. Milk, which contains all the elements of a proper food in convenient form, has for long been esteemed the ideal diet for such a condition, and yet with patients on the milk diet as ordinarily practised loss of weight has been a striking feature of most cases of the disease. From a large series this loss has been estimated to amount to 200 to 600 grams daily (7 to 20 ounces), made up of water, fat, and the protein of body tissues, the greater part probably coming from the destruction of body tissue. By determining the amount of nitrogen in food, feces, and urine, it is in general easy to learn how much protein is absorbed from the food supply, and how great is the protein loss from the body tissues. In a table of statistics of 178 experiments collected by Nichols,[3] it is well shown that an insufficient supply of food nitrogen results in poor absorption and extensive nitrogen loss, while with a more liberal supply of nitrogen (16 to 20 grams) about 88 per cent. is absorbed, and the nitrogen loss is reduced to a minimum of 3.7 grams per day. Practically this means that starvation is the greatest cause of the loss of body weight, and that sufficient food would prevent to a great extent the loss of weight.

Exactly how much of the emaciation is due to the pyrexia or to the toxemia or to both is difficult to estimate, although it is known that by artificially raising the body temperature an increase of protein metabolism does occur. On the other hand, it has also been shown both in laboratory and bedside experiments that an increase in the diet will decrease protein destruction even in fever, and the opinion of most investigators is that a more liberal diet prevents to a great extent the protein loss due to fever as well as that due to starvation.

That the ordinary typhoid-fever diet does not prevent this emaciation is evident, and the reason is clear. A normal resting individual weighing 70 kilos (150 pounds) and receiving sufficient food expends about 33 calories per kilo of body weight per day, or a total of 2300 calories. In fever there is approximately an increased heat production of 25 per cent., which added to the 2300 calories makes 2800 calories. If a fever patient does not have this amount of energy supplied in his food he will burn up his own tissues to supply the deficit. If he receives 1500 to 2000 c.c. of milk per day, as in the ordinary milk diet, he receives about 1000 to 1400 calories only. The

[3] Diet in Typhoid Fever. Fiske Fund Prize Dissertation No. 50, Providence, 1907 (contains complete bibliography).

liquid diet, of which milk is always the main constituent, has about the some caloric value. If all typhoid subjects were to get 3 to 4 liters of milk daily the problem of typhoid-fever feeding would be simple, but for many very obvious reasons this is impossible, and we must look for additional food to supply the deficiency.

It is almost a traditional belief in medicine that milk and other liquids are the most easily digested and absorbed, as well as the least likely to excite harmful peristalsis in the inflamed intestine, but there is certainly not sufficient evidence to prove this assertion. As a matter of fact, experiments performed on typhoid fever patients during the febrile period of the disease show that the absorption of most easily digested foods, including milk, is on the average 5 to 10 per cent. less than in a normal person. Further, excluding foods with a heavy vegetable residue it is impossible to prove that food, such as an egg or a piece of meat, will reach the inflamed Peyer's patches in more solid form than milk which enters the cardiac orifice of the stomach a liquid and leaves the pylorus a solid.

But, after all, the proof of the typhoid diet is in the eating, and we must look to actual results of various diets for the final test. Barrs,[4] in 1897, wrote about a less restricted diet that "it is likely to modify favorably the death rate, to shorten convalescence, to diminish the risks of complications and sequelæ, and to make typhoid fever a less formidable and more manageable disease than it is under our present standard methods of treatment." Before and since that time observations have been made by clinicians in various countries with diets varying from the mere addition of soft eggs or soft toast to one containing meat, and as far as I have been able to determine not a single adverse report has come from any observer who has had the courage to try a more liberal diet. In this country Shattuck[5] was the first to point out the advantages of a more liberal diet, and Thayer,[6] by calling attention to the excellent results obtained by certain Russian investigators, stimulated further active interest in the subject. Litchfield[7] also has recently written on the subject. Kinnicutt[8] collected the available statistics up to 1906, with the results seen in Table I.

TABLE I.

No. of cases.	Relapses.	Per cent.	Hemorrhages.	Per cent.	Perforations.	Per cent.	Deaths.	Per cent.	
733	48	11.3	35	4.7	10	1.3	60	9.4	Liberal diet.
4654	507	10.8	411	8.8	111	2.4	491	10.5	Liquid diet.

[4] A Plea for a Less Restricted Diet in Typhoid Fever. Brit. Med. Jour., 1897, i, 125.
[5] Diet in Typhoid Fever. Jour. Amer. Med. Assoc., July 10, 1897, p. 51.
[6] Progressive Medicine, 1899.
[7] Nourishment of Patients during Typhoid. Penna. Med. Jour., October, 1908.
[8] Principles of Feeding in Typhoid and in other Fevers. Boston Med. and Surg. Jour., clv, i, 1.

It is seen that the death rate is lower, there are fewer perforations and hemorrhages, and a slight increase in relapses in those cases liberally fed.

An analysis of the cases treated at the Johns Hopkins Hospital from July, 1906, to July, 1908, inclusive, to which I am allowed to refer by the courtesy of Professors Barker and Thayer, shows the following results (Table II).

TABLE II.

	No. of cases.	Hemorrhages, per cent.	Perforations, per cent.	Relapses, per cent.	Abdominal pain, per cent.	Nausea, vomiting, per cent.	Distention, per cent.	Hypothermia, per cent.	Tachycardia, per cent.	Deaths, per cent.
Series I. Liberal diet.	98	13.3	3.0	18.3	26.5	15.3	7.0	44.3	51.1	6.1
Series II. Liquid diet.	149	16.7	3.3	12.7	30.8	17.4	9.4	53.1	42.0	12.7

The 149 cases in Series II include about 75 who received only milk and albumin water, approximately from 700 to 1000 c.c. of each daily, a few extremely ill cases who received albumin water only, and about 70 who had broths in addition. The 98 cases of the first series include all patients who were given, during the febrile period, any soft or semisolid food—some received simply one soft egg three times a day in addition to liquids, others got also soft toast, but most were allowed the choice of eggs, toast, thin gruels, custard, junket, and jelly. There was no rule of selection of cases, but patients who were extremely intoxicated on entering the hospital generally would not take more than liquids. This probably means that, on the whole, the fed cases were slightly milder than those of Series II. Both series include cases from all seasons of the year, the patients were from the same walks of life, and were given identical treatment except for the diet. In all cases water was freely given. Both tables show that there is no justification for the fear felt by some about the possible increase of complications following more food, and with the exception of the increase in relapses the results are all in favor of a freer diet. In the Johns Hopkins cases the deaths in Series I were due in three instances to perforation, in two to toxemia, in one to hemorrhages; one patient was in the hospital only two days before the exitus. To avoid unfair comparisons the deaths in Series II must be explained. Six patients were in the hospital from one to six days before dying: one from acute nephritis, one from typhoid meningitis associated with general peritonitis due to a gangrenous appendix, four from the extreme toxemia. Further, one death was due to intestinal strangulation caused by adhesions from an old gynecological operation. Of the 12 remaining, 4 died from

perforation, 1 from a scrotal abscess, 1 from pneumothorax, and 6 from the effects of the toxemia. Therefore, one is not by any means justified in concluding from these comparative death rates that a more liberal diet lowers the mortality 50 per cent. The incidence of hemorrhage and perforation is less; the rather large difference in the number of relapses was surprising, but the small number of cases may easily account for this. As relating to the digestibility of the respective diets, it is interesting to note that abdominal pain, nausea, vomiting, and distention are present to a less degree in Series I than in Series II. Diarrhœa is such an uncommon feature of typhoid fever at the Johns Hopkins Hospital that notes on its very occasional presence have no value in the present analysis. Hypothermia was distinctly less marked in Series I, not only in percentage values, but also in the degree to which it was present in the individual cases. The increase in the percentage of tachycardia is possibly due to the fact that the patients of Series I were let out of bed earlier.

In order to determine any possible effect of diet on the length of the disease, calculations were made of the average length of pyrexia and of duration of illness. The results are expressed in Table III.

TABLE III.

	Duration of fever.	Duration of illness.	Convalescence.	
Series I. Liberal diet.	34.2	52.4	18.2	Days.
Series II. Liquid diet.	32.9	53.0	20.1	

Only those patients who recovered were included in this list. The temperature was considered normal only when it was 99° in the rectum for a whole day and remained so. In case of relapse, the first day of normal temperaure following the relapse was used in the calculation. It is seen that in the cases fed the duration of pyrexia was slightly longer, as is to be expected from the increased number of relapses; but the total length of the illness is shorter, and convalescence is almost two days less.

In typhoid fever results may follow certain lines of treatment, not because of the treatment, but rather as co-incidental happenings: consequently, results such as these must be accepted conservatively. Certainly physicians who have treated patients in both ways agree that convalescence is less formidable; that the necessary increase in diet during convalescence is a far easier task; that the patient is much more comfortable; and that his general condition is better after an attack of typhoid during which his dietary is "liberal." Such a liberal diet has been tested sufficiently to warrant the conclusions not only that it is not harmful, but that it offers distinct advantages over the low diet. The distressing hunger and extreme emaciation are

symptoms which can be prevented in most cases; and with care in the selection of food we should not only be able to do this, but we should also be able to stimulate the psychic factor of digestion and thus allow of better absorption than is possible with distasteful food. It still remains for the hospital laboratory to determine the ideal proportions of fat, carbohydrate, and protein in a typhoid-fever diet. Schaffer's[9] recent work with a high carbohydrate ratio is most suggestive. Although the chemical composition and the caloric value of any food can be found in published tables, for general purposes outside of hospitals it is sufficient to choose a dietary from a wide variety of digestible foods, such as has been used by Shattuck (appended below). No absolute rules can be laid down, and all patients cannot be freely fed. A hospital physician can order articles of diet for his typhoid-fever patients which a country practitioner would find absolutely impracticable. The question is not of a choice of solid or liquid food, but of sufficient food selected so as best to supply the wants of the organism without harming the patient.

The conclusion drawn from this study is, that, while details of diet cannot be prescribed by dogmatic rules, the underlying principle in feeding typhoid fever patients should be to furnish at least the same amount of food energy required by a healthy resting person.

Shattuck's Dietary: Milk, hot or cold, with or without salt, with lime water, soda water, Apollinaris, Vichy; peptogenic or peptonized milk; cream and water; milk with white of egg and slip; buttermilk; koumyss; matzoon; whey; milk with tea, coffee, cocoa.

Soups: Beef, veal, chicken, tomato, oyster, mutton, pea, bean, squash, carefully strained and thickened with rice, arrowroot, flour, milk, egg, cream, barley.

Horlick's, Mellin's, malted milk, carnipeptone, bovinine, somatose, beef juice.

Gruels: Strained cornmeal, crackers, flour, barley water, toast water, albumin water, lemon water.

Ice cream.

Eggs: Soft boiled, raw, eggnog.

Finely minced lean meat, scraped beef, soft part of raw oysters, soft crackers with milk or broth, soft puddings without raisins; soft toast without crust; blanc mange, wine jelly, apple sauce, macaroni.

[9] Metabolism in Typhoid. Jour. Amer. Med. Assoc., September 19, 1908, p. 974.

TYPHOID BACILLURIA.

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FOR many years typhoid fever has been known as a disease which occurs with varying frequency, sometimes assuming the proportions of serious epidemics, again becoming rare, but seldom entirely absent from populous regions. With the discovery that the fever is due to a definite and recognizable bacterium, it seemed as though the disease could be checked by measures designed to prevent the dissemination of the organism from the patient. The first measures were taken to prevent dissemination by the feces, in which the bacillus was early discovered. Then it became apparent that through the urine, too, the bacillus is spread, and measures were taken to disinfect this excretion. However, even with the most careful disinfection of all excretions, and vigorous sanitary supervision of water and food supply, cases of typhoid fever continued to develop. Of late, the important observation has been made that a person who has recovered from typhoid fever, or even a person who has never clinically manifested the disease, may carry in his body for months and years virulent typhoid organisms and continue to infect the community. The gall-bladder, the intestinal tract, and the urinary bladder have all been found to harbor the bacilli in great numbers. Additional measures against these foci of infection now occupy the attention of preventive medicine and sanitation. This paper will consider only the occurrence and the control of typhoid bacilli in the urine.

In 1881 Bouchard found in the urine of typhoid fever patients bacilli similar to those discovered the year previous by Eberth in the spleen and mesenteric glands. He examined the urine of sixty-five patients, and demonstrated the bacilli in twenty-one cases. His observations have since been repeated and elaborated by a number of observers. But the present attitude of science toward the occurrence of typhoid bacilli in the urine must be based chiefly on the observations of the past twelve years. The results of even the most careful earlier researches are not reliable, for not until 1896 did the development of the knowledge of serum agglutination and the improvement in bacteriological technique admit of accurate differentiation between the colon and allied groups and the typhoid organism. Therefore, this article deals principally with recent observations.

I have been interested in the occurrence of typhoid bacilli in the urine for some years. When on the house staff of the New York Hospital, in 1902, I studied a series of fifty consecutive cases of

typhoid fever, and found the typhoid bacillus in the urine of eleven cases. Since that time certain laboratory work has been done bearing on the appearance and disappearance of the organism. In this paper I will, first, summarize my own cases; second, discuss the clinical and laboratory observations of the various investigators which bear on the occurrence of typhoid bacilli in the urine, incorporating in this discussion the details of my own work; and, third, consider the treatment of typhoid bacilluria.

Summary of Personal Cases.[1] At the New York Hospital, from August to December, 1902, 50 consecutive cases of typhoid fever were followed by urine cultures from the time of their admission to the hospital into the third week of convalescence. Cultures were taken every three to six days; in 197 examinations catheterized urine was used; in 126 others the urine was passed by the patients. One cubic centimeter of urine was caught directly from the stream into each of two 10 c.c. tubes of bouillon, and into several empty tubes for observation and analysis. The urine of these 50 cases was also studied by numerous gross and microscopic examinations. Several other cases were followed for periods until proved not to be cases of typhoid fever.

The bacterial findings in the 323 examinations were:

Typhoid bacilli (pure)	47
Typhoid bacilli and cocci	6
Typhoid bacilli and colon	1
Staphylococci	36
Streptococci	11
Diplococci (?)	4
Colon bacilli	7
Proteus	6
Hay bacillus (?)	3
Mixed bacilli	9
Number of times sterile	193

The cocci were largely contaminations from the urethra in cases which had previously had, within two years, a urethritis. In one case streptococci faintly clouded the catheterized urine. This Streptococcus bacteriuria was unaccompanied by symptoms and quickly disappeared spontaneously. One case of persistent Colon bacilluria was present in a male patient at the first and three subsequent examinations. Otherwise, the colon, the proteus, and the mixed infections were traceable to catherization, other than the clean catheterizations of this series.

The bacilli tabulated as typhoid were accepted when they grew out actively on the first or second transfer in bouillon, produced no indol, produced no gas in glucose agar, and did not change litmus

[1] I desire to express my indebtedness to Drs. George L. Peabody and Samuel W. Lambert, attending physicians to the New York Hospital, for the use of the clinical material of this series, to Dr. Louis Hamman, former house physician, for suggestions and assistance, and to Drs. William J. Elser and J. C. Roper, for suggestions and for the use of the laboratory of pathology.

milk, and were completely agglutinated within five minutes at a serum dilution of 1 to 50.

TOTAL, FIFTY CASES.

No.	Age.	Sex.	Type.	Eruption.	First culture.	Albumin.
11	12–20	Male, 39	Fatal, 3	Marked, 11	1st week, 16	Heavy, 2
17	21–25	Female, 11	Severe, 14	Moderate, 12	2d week, 22	Moderate, 2
12	26–30		Moderate, 17	Scanty, 20	3d week, 8	Scanty, 31
9	31–40		Mild, 16	No spots, 7	4th week, 4	None, 15
1	45		Relapses, 10			

POSITIVE CASES.

Serial No.	Age.	Sex.	Type.	Eruption.	First culture.	First positive.	Known duration.	Albumin.	Pus.
5	45	Male	Severe	+	17th day	17th day	17th day 29th day to 59th day	0	+
6	27	Male	Moderate relapse	+	21st day	28th day	28th day to 50th day	+	+
19	21	Male	Severe	++	11th day	27th day	27th day to 41st day	+	0
24	29	Male	Severe relapse	++	14th day	63d day	63d day to 79th day	+	0
28	27	Female	Severe	+	11th day	20th day	20th day to 34th day	+	+
33	14	Male	Severe relapse	+	11th day	22d day	22d day to 32d day	0	+
34	38	Male	Mild	++	5th day	17th day	17th day to 39th day	+	0
36	21	Male	Severe	+	13th day	24th day	24th day to 81st day	0	0
38	23	Female	Moderate	Scant	9th day	19th day	19th day to 43d day	0	+
41	30	Male	Fatal	+	7th day	10th day	10th day	+	0
49	12	Male	Severe relapse	++	7th day	24th day	24th day to 48th day	0	+

FREQUENCY OF TYPHOID BACILLURIA. In determining statistically the frequency of this condition, it was at once seen that a grouping of the various series of observations was imperative, and that the percentage of the frequency of typhoid bacilluria, to be approximately correct, owing to the frequent errors in cross references, should be based only upon original articles personally reviewed.[2] The series accepted comprises apparently consecutive and unselected cases[3] of typhoid fever, sufficiently examined to detect any lasting

[2] I could not find the original papers of these series:

Year.	Name.	Number examined.	Number positive.
1897.	Levy and Gissler	22	10
1901.	Gualdi	105	51
1901.	Ischikawa and Kaharhi	24	15

[3] The following are not included in the statistics, being selected or special groups of cases, and therefore not a fair average:

Year.	Name.	Number examined.	Number positive.
1900.	Horton Smith (selected cases)	6	6
1903.	Flamini (children)	8	7
1899.	Schichhold (severe cases)	17	5
1897.	Besson (nephritic cases)	33	6

bacilluria,[4] and of such type[5] and recent period[6] as to make the identifications of the bacilli trustworthy.

Based on the following 621 cases, of which 150 showed typhoid bacilli in the urine, it may be stated that typhoid bacilli can be detected in the urine of 24 per cent. of all cases of typhoid fever.

Year.	Name.	Number examined.	Number positive.
1897.	Horton Smith	7	3
1898.	Richardson	38	9
1899.	Richardson	66	14
1899.	Horton Smith	12	4
1900.	Neufeld	12	3
1900.	Horton Smith	39	11
1901.	Vincent	46	9
1901.	Shuder	22	5
1901.	Klimenko	65	13
1902.	Jacobi	35	7
1902.	Fuchs	41	4
1903.	Sato	17	11
1904.	Herbert	98	18
1905.	Lesieur and Marchand	26	11
1906.	Brown	15	8
1906.	Lesieur	6	3
1907.	Vas	26	6
	Connell.	50	11
		621	150

[4] It does not appear that these cases were sufficiently examined:

Year.	Name.	Number examined.	Number positive.
1898.	Petrusky (not followed for per cent.)	50	3
1901.	Lewis (technique in doubt)	45	1

[5] In these cases the identity of the bacilli was not determined:

Year.	Name.	Number examined.	Number positive.
1902.	Bliss	311	31
1904.	Knox	100	51

[6] The following are excluded because of having been reported prior to the period of accurate differentiation of the typhoid bacillus:

Year.	Name.	Number examined.	Number positive.
1881.	Bouchard	65	21
1886.	Seitz	7	2
1886.	Wyssokowitsch	7	2
1886.	Hueppe	18	1
1887.	Berlioz	14	2
1889.	Konjajeff	20	3
1888.	Neumann	23	6
1890.	Neumann	48	11
1890.	Karlinski	44	21
1892.	Silverstrini	7	7
1892.	Enriquez	12	7
1894.	Borjes	10	2
1895.	Barte de le Falle	27	4
1895.	Wright and Semple	7	6
1895.	Blumer	10	2
1895.	Melchior	4	1

From the standpoint of preventive medicine, of more importance than the mere percentage of bacilluria is the number of bacteria present, and the time and duration of their occurrence.

THE NUMBER OF BACILLI. The bacilli are usually found in enormous numbers, often so many being present as to render the urine turbid. The actual count of bacteria varies greatly from day to day and from hour to hour, but often runs into the millions and occasionally into the hundred of millions of organisms to the cubic centimeter of urine. Petrusky found 172,000,000 bacilli to the cubic centimeter in one case; Gwyn estimated 500,000,000 to the cubic centimeter in another. Less frequently the bacilli are found in scant numbers, sometimes averaging even less than one bacillus per cubic centimeter of urine (Jacobi, Besson, Connell). Some few writers (Fuchs, Schichhold, Flamini) have found the bacilli few in number in most of their positive cases.

TIME OF OCCURRENCE. The bacilli invade the urine and are detected most frequently in the declining stage of the disease, at about the time when the temperature reaches normal. Several early observers recovered bacilli, supposedly typhoid, from the urine in the first few days of the disease. Possibly these observers were dealing with proteus or colon contaminations, as no recent observer has confirmed their findings. However, Pavlovsky has demonstrated experimentally the probability of a "period of distribution" prior to the actual febrile invasion of various diseases. His investigations have shown the quick excretion of typhoid bacilli in the urine supposedly by the eliminative efforts of the renal epithelium.

As to the earliest appearances recorded by recent observers, Schichhold, out of six cases of bacilluria, found the earliest infection of the urine on the seventh day. Jacobi, in eight cases, found the earliest infection on the eighth day. Lesieur and Marchand state that in three of their eleven cases bacilli were found first on the minth, tenth, and eleventh days respectively.

In one case of my series, on the tenth day of the illness, I recovered the typhoid bacillus from one of two bouillon tubes, each planted with 1 c.c. of urine.

Horton Smith, in 17 cases, found the earliest infection on the thirteenth day; Richardson, in 9 cases, on the fifteenth day; Neufeld, in 3 cases, on the twentieth day; Shuder, in 5 cases, on the twenty-fifth day; Brown, in 8 cases, on the twenty-eighth day. The usual time of onset of bacilluria has been after the third week of the fever.

The finding of the bacilli in the urine has been more constant in relation to the temperature curve than to the day of disease. In Richardson's nine cases of bacilluria, the bacteria were first found in the various cases from a few days before the temperature reached normal to a week after; in Shuder's, from a week before to three weeks after; in Petrusky's, from a few days before the fall of temperature until ten days after; and in Brown's eight cases the earliest

finding varied from a week before to two weeks after normal temperature had been reached. A few careful observers of limited series, such as Jacobi, have found the majority of infections to occur first during the stage of fever. No doubt with many observers the bacteria often escape detection at this period, for when found during the febrile stage the number of bacteria has usually been scanty and their duration in the urine brief. In a few cases the first appearance of the bacilli has been during a relapse. Analyzing the cases reported by the various observers, it may be stated that, as a rule, the bacilli first appear in the urine from one week before to two weeks after the temperature has reached normal, most commonly within a few days of the first day of normal temperature.

Of my positive cases, if we exclude the one mentioned in which a stray bacillus was recovered from a single tube on the tenth day of fever, none of the remaining ten occurred during the stage of high continuous temperature. One case was positive on the seventeenth day in the stage of steep curves; the remaining nine were first positive in the period from eight days before to eight days after the temperature had reached a continuously normal line.

Duration. The bacilli usually persist in the urine for several weeks and disappear spontaneously in most instances. However, a considerable proportion of cases continue long into the ambulatory stage, sometimes for years, rendering the patient a grave menace to public health. Not many observers have followed these cases for the purpose of noting how long the condition may continue. Richardson followed 7 cases, 2 of which cleared up in the hospital; the other 5 left the hospital with their urine swarming with typhoid bacilli. Petrusky followed 3 cases, in which the shortest duration was eight days, the longest was three months. Shuder's and Fuchs' cases were of brief duration. Horton Smith followed 5 cases, finding the shortest duration eight days, the longest seventy days. Sato's cases lasted from eight to forty-two days.

Of my 5 untreated and non-fatal cases, the shortest duration was fourteen days, the longest forty-two days. In 4 cases the bacilluria was terminated by treatment, on the fourteenth, sixteenth, twenty-fourth, and fifty-seventh days of their duration. One patient died.

Longer duration of the bacilluria is not uncommon. Rousig examined sixteen German soldiers returning from the siege of Pekin six months after their attacks of typhoid fever, and found the urine of one swarming with typhoid bacilli. Houston found typhoid bacilli present in the urine in pure culture at the end of three years, and Young followed for two years a patient who had wandered seven years since his attack of typhoid fever, a menace to the whole community; and Liebtrau reports among other cases of typhoid carriers one who after nine years showed typhoid bacilli in the urine.

CONDITIONS DETERMINING THE OCCURRENCE OF TYPHOID BACILLURIA. The generally accepted theory to account for the number and continuance of typhoid bacilli in the urine is that the urine, having become infected from the blood by a few organisms, serves as a culture medium. It is not reasonable to suppose that all or even any large number of the bacilli existing in the urine are eliminated from the blood by the kidney, considering, first, the relatively small number of bacteria in the circulating blood even during the height of the disease; second, the fact that the usual period of bacilluria occurs at a time when no organisms can be detected in the blood; and third, that a bacilluria may be terminated in most cases by antiseptic irrigation of the bladder. For instance, Horton Smith found no bacilli in the blood of four cases which showed in the urine enormous numbers of bacilli. The same result was obtained by me in two cases. Gwyn and Richardson found that vesical irrigations of mercuric chloride terminated the bacilluria; and I have used irrigations of silver nitrate successfully. Therefore, no considerable number of the bacteria in the urine are direct eliminations from the blood.

CHANNELS OF INFECTION. That infection of the urine can occur by the urethra seems proved by a patient of Brown, who developed a pure typhoid bacilluria and cystitis by infection from a catheter. Lesieur has experimentally demonstrated this mode of infection in dogs. The bacilli so planted multiplied and persisted for a month or more. That infection by the urethra is the usual mode is highly improbable, as is, also, the theory suggested by Blumer, that the bacterium finds its way from the rectum through the posterior vesical wall. Nor are cases of suppurative foci of the genito-urinary tract, such as Flexner's case, sufficiently common to furnish an adequate source of urine infection. In 289 postmortem examinations on typhoid fever cases, Horton Smith reported that in only one case were there suppurative foci of the kidney that would account for bacilli in the urine. The generally accepted theory of the mode of infection is that a bacillus finds its way from the blood stream, through the kidney, into the urine, and is washed into the bladder; and there, finding in certain cases a stopping place and a satisfactory culture medium, it proliferates.

The bacilli probably exist in the blood in all cases. They are recoverable in a high percentage, 75 per cent. of the 1602 cases collected by Coleman and Buxton. The bacilli have been repeatedly recovered postmortem from the kidney, as from other organs. That the kidney excretes bacteria, or permits their passage has been experimentally proved by Pavlovsky. Especially the excretion is profuse in the stage of distribution before body resistance is manifested by symptoms of disease. In pyogenic and pneumonic infections, as well as in typhoid, the specific bacteria have been recovered from the urine. It is a moot question whether the elimination

of bacteria is a normal kidney function, or is dependent on renal damage, be it ever so minute and localized. I am inclined to the latter view.

The kidney presents, histologically, interstitial lymph nodules and an immense vulnerable capillary network, in which structures septic typhoid emboli are demonstrated in many instances. At the New York Hospital laboratory of pathology, minute focal necroses are frequently found in the kidneys of severe cases of typhoid fever.

At least temporary damage to the renal epithelium, as evidenced by the coarse laboratory determinations of albuminuria, is the rule at some stage of the long-continued typhoid intoxication. (Besson, found 47 cases positive for albumin out of 77; I, 35 positive out of 50.) However, detectable damage does not seem necessary, for a single lesion in a glomerulus or tubule would seed the urine as effectually as a gross nephritis; yet this damage would not be expressed by detectable albumin. That these minute local lesions must be of frequent occurrence even in healthy individuals is evident to anyone who has searched earnestly for histologically perfect renal tissue. Lesions elsewhere in the urinary tract, when such occur, would also allow, equally as well as renal lesions, the egress of the bacilli from the blood.

The microörganisms do not usually persistently infect the entire urinary tract, but become localized in the bladder. This has been proved by Richardson, Gwyn, and me, in cases terminated by antiseptic vesical irrigation, showing that the bacilli were local in the bladder, and also in Horton Smith's case, in which a culture from the bladder and kidneys, postmortem, showed that in this case the bladder urine alone was infected.

The Urine as a Culture Medium. Merkel and Goldschmitt, among the early investigators, demonstrated that typhoid bacilli could multiply in the urine in the test-tube, especially when this was weakly alkaline or neutral. Horton Smith, in 1900, inoculated six specimens of urine. The bacilli grew profusely in four, scantily in two. Park, in 1901, inoculated forty-five specimens of urine with those bacteria, other than the typhoid bacillus, which commonly infect urine. The growth varied, dependent chiefly on the acidity of the urine. For these other organisms (Colon bacillus, streptococcus, etc.) he found that high degrees of urine acidity inhibited growth.

To determine why the typhoid bacillus thrives in certain urines only, I took three tubes of typhoid urine in each of forty consecutive catheterizations. One tube was planted with a loop of bouillon culture of typhoid, two were held as controls, and were incubated for forty-eight hours. Of these forty sets, nine were discarded because of contaminations, and four because of obscuring phosphatic precipitates. The growth and analysis in the remaining twenty-seven were noted.

In 6 of the 27 specimens the bacilli multiplied so rapidly as to cloud the urine in twenty-four hours. This increase was about half as rapid as in bouillon similarly inoculated. Most of the organisms were sluggish or non-motile; a few were actively motile. In 9 of the 27 specimens the growth gave a faint cloud of bacteria in forty-eight hours. Twelve remained unclouded. However, even these latter, on examination in hanging drop, showed a considerable increase in the number of sluggish and non-motile typhoid bacilli over the original number planted. The organisms were roughly proved in each case by transfer to litmus milk and by prompt agglutination at a serum dilution of 1 to 50.

To summarize the more important observations on these 27 specimens: In specific gravity, six specimens were below 1012. In all of these the bacteria clouded the urine within forty-eight hours. Sixteen varied from 1012 to 1024. In 9 of these the bacteria clouded the urine; in 7 there was no clouding. The remaining 5 specimens were above 1024 in specific gravity. All these remained clear.

As to albumin content, of the 22 specimens which were below 1024 in gravity, 6 specimens contained albumin. Of these, 4 were good media, 2 were poor. Of the five urines above 1024, 2 contained heavy traces of albumin. Both were poor media. Albumin seemed from these observations to be no important factor in the growth of the organisms.

The acidity of the twenty-seven urines was determined by titration with decinormal sodium hydrate, using litmus as an indicator. The urines in which the organisms grew best were weakly acid, neutral, or alkaline to litmus. The more acid urines showed only a slight growth. Even the most acid specimens were merely inhibitory, not bactericidal, for from three of these highly acid urines, kept at room temperatures, living typhoid bacilli were recovered two months after inoculation. It seemed evident from these observations that the most important factor in determining cultural conditions was the degree of acidity of the urine. Therefore, I have recently (1906–1908) inoculated a series of urines to determine the degree of urine acidity influencing typhoid growth.

The specimens used were albumin-free urines, thirty-eight in number, freshly passed by normal individuals who were not receiving any medication. Ordinary analysis was made of the urine, then the acidity was determined by n/10 NaOH, using phenolphthalein as an indicator.

The urine acidity expressed in percentage of n/10 NaOH ranged from 4 to 112 per cent. No urine tested was neutral or alkaline to phenolphthalein, although some of the urines of low acid percentage by phenolphthalein were neutral or alkaline to litmus.

Ten c.c. of filtered sterile urine was planted with a loop of twenty-four-hour bouillon culture of typhoid bacilli, and kept at

38° C. for two days. The growth was noted in hanging drop and given an approximate index, using 100 as a basis for those urines in which the growth was best. In the urines given the highest rating the bacteria developed in forty-eight hours to about the same extent as they do in bouillon in twelve hours. The results noted follow:

Per cent. of urine acidity in terms of n/10 NaOH.	Growth index.	Per cent. of urine acidity in terms of n/10 NaOH.	Growth index.
4	100	28	10
4	100	30	10
7	100	33	10
8	100	36	5
9	30	38	10
10	100	40	0.5
10	10	50	1
12	100	52	15
12	20	53	10
12	50	54	0.5
14	40	60	4
15	80	66	3
15	10	73	0
15	80	80	0.5
16	40	87	2
17	100	90	3
18	80	110	2
22	80	110	0
26	80	112	0.5

Of the above urines, in those of low acidity, that is, below 20 per cent. n/10 NaOH, the bacteria usually throve. These were straw colored, or light amber urines, below 1018 in specific gravity. In the urines of medium acidity, that is, 20 to 40 per cent., the bacilli were inhibited in growth to variable degrees; and in the highly acid urines they were markedly inhibited.

To make sure that such inhibition was not due to lack of food, two of these strongly acid urines were diluted one to four with water, sterilized by filtration, and inoculated. In these diluted specimens the bacilli grew luxuriantly, whereas in the undiluted specimens the growth was scanty.

It was further determined that the inhibition was not due to the neutral saline contents, for on partially neutralizing the acidity of the urine by the addition of concentrated sodium hydrate, in four acid urines of poor cultural character, the urines became good media for the growth of the bacilli. The inhibition seemed due, therefore chiefly to the acid contents of the urine.

However, it was found that the degree of inhibition did not bear a constant relation to the degree of acidity; for instance, one urine of an acidity of 10 per cent. had a growth index of 100, and another of the same percentage, a growth index of only 10; also in the experiments in reducing acidity by sodium hydrate, it was found that a urine of an acidity of 112 per cent. reduced to an acidity of 90 per

cent. had a growth index of 60, whereas a urine of natural acidity of 90 per cent. had a growth index of only 3. It, therefore, seemed probable that the inhibitory factor was not the total acidity, but some particular acid or group of acid bodies.

To determine what the inhibitive acidity was, I made further observations. Acid sodium phosphate was first experimented with. Urines of low acidity (6 specimens) which grew the typhoid bacillus well were acidified with acid sodium phosphate to 20, 40, 60, 80, and 100 per cent. n/10 NaOH. At 60 per cent. one specimen showed moderate inhibition; at 80 all specimens showed moderate, and at 100, complete, inhibition. From the large amount of sodium phosphate needed to inhibit growth, it was evident that this was not the inhibitory substance in those urines which showed marked inhibition when the natural acidity was 30 to 40 per cent. n/10 NaOH.

Organic acid then suggested itself. Acetic and lactic acid as types of feeble dissociating organic acids were added to 6 urines of low acidity and good cultural character. At 2 per cent. n/10 NaOH these acids were markedly inhibitory, and at 15 to 20 per cent. were absolutely inhibitory to growth of the typhoid bacillus. The same results were obtained with uric acid in minute quantities.

Folin has shown that a high and varying percentage of urine acidity is due not to sodium acid phosphate, but to organic acids, for the most part of undetermined nature. These in certain of his specimens accounted for more than 50 per cent. of the total acidity. Paus has proved the inhibitory effect of the amino, oxybutyric, and other acids identical with or allied to the organic acids of the urine; these acids, in strengths of 0.2 to 0.3 per cent., are as absolutely inhibitory to the growth of typhoid bacilli as acetic and lactic acids, and one-third to one-half as inhibitory as the dissociating mineral acids, such as hydrochloric. These observations warrant the conclusion that the inhibitory factor in the urine is usually the organic acidity, which, when in excess prevents the growth of the typhoid bacillus.

It is known that in fever, metabolism is much increased and the nitrogenous output is excessive. The usual acidity, as I determined in titrating over two hundred typhoid fever urines, ranges in the high febrile stage from 30 to 80 per cent. n/10 NaOH, with an average of about 40 per cent.; in the declining and post febrile stage, the range is 4 to 30 per cent., with an average of about 12 per cent.; and in the stage of active convalescence, 4 to 50 per cent., with an average of about 20 per cent. To the high acidity of the febrile stage, and possibly to a high ratio of organic acidity, I attribute the infrequency of bacilluria and the small number of bacilli and the short duration of bacilluria at this stage. In the declining and postfebrile stage, cultural conditions are improved by the dilution of the urine and low acid output. If in the urine,

which is a good culture medium at this stage, the bacterium appears, it proliferates enormously, particularly if there be a trace of albumin present.

In evidence of the low organic acidity of this latter stage, Roper has found at the New York Hospital, in a series of total nitrogen determinations on the urine of convalescent typhoid fever patients, that in the post-febrile stage the uric acid falls to a negligible quantity.

To determine if enriching the urine by the addition of serum albumin modified the inhibitory effect of urine acidity, faint traces were added to twelve urines of varying acidity. The reduction of acidity by such addition was so slight (1 to 2 per cent.) as to be negligible. Serum albumin added to diluted, faintly acid urines considerably increased the value as culture media for typhoid bacilli. Added to more acid urines, the albumin was without appreciable effect. The conclusion from this limited series is that while albumin acts as a food for the bacteria, the increased value to the urine as a culture medium is not marked enough to mitigate the inhibitory effect of excessive acidity.

Residual Urine and Stasis. The bacteria, in addition to finding a favorable medium for growth, must find a resting place, else they will be mechanically expelled from the urinary passages by the outflow of urine. This factor in the establishment of an enduring bacilluria, a certain degree of stagnation of urine in the bladder, seems to be particularly favored by the nature of typhoid fever. The period of illness is long, the muscle tone poor, the patient apathetic, the bladder often distended and incompletely evacuated. Hence, in the latter stages of the disease, when the urine becomes a favorable medium, any typhoid organism coming down the ureter finds in the urinary bladder a stopping place, from which it is not expelled until it has many times multiplied and effectually seeded the bladder urine.

During the height of the fever the bladder is often overdistended. The clinician not infrequently finds the bladder of the apathetic or delirious patient reaching half way to the umbilicus, distended by 20 to 30 ounces of urine. This partial retention is often overlooked; it yields to expectant measures, and is not considered worthy of note. Yet the effect of such overstretching of weakened muscle layers must reach far into the convalescence and must frequently result in residual urine. That retention does not more frequently lead to immediate bacilluria must depend on the inhibitory effect of the acid urine of the febrile stage, rather than on an assumption, proved to be erroneous, that bacteria do not escape into the urine at this stage.

The influence of retention was investigated by Bliss. In following 311 cases, he observed 39 who suffered from retention. 23 per cent. of these cases developed later a bacilluria, while only 8 per cent.

of those cases which had had no retention developed urine infection. Retention occurred as an early symptom; the bacilluria late.

My attention was particularly directed in one case to the possibility of retention as a predisposing cause of bacilluria. This patient, a young adult male, had suffered from retention in the height of the disease. Treated for bacilluria in the ambulatory stage of typhoid fever, the condition failed to yield to an eight day's course of urotropin. Although the bacilli diminished promptly, they did not entirely disappear. He was, therefore, catheterized for purposes of bladder irrigation. On inserting the catheter directly after completed urination, four ounces of residual urine was found in the bladder.

Subsequently, three other bacilluria cases were similarly catheterized for residual urine. One had only a normal amount of about 1 dram; one had over 1 ounce; and one about 5 ounces. It is clear that residual urine would invite and harbor the growth of typhoid bacilli as it does the growth of other bacteria, as in colon, proteus, and streptococcic infections of the urine, which are not at all uncommon in typhoid fever patients.

Type of Typhoid Fever. The bacilluria occurs most frequently in severe types of typhoid fever, particularly in the complicated and relapsing types. This has been the uniform experience of all the observers except Klimenko. Of my 50 cases, 3 were fatal, 14 severe, 17 moderate, 16 mild. Of the 11 bacilluria cases, 1 was fatal, 6 severe, 2 moderate, 2 mild. This gives 63 per cent. of severe and fatal cases in the bacilluria series, against 34 per cent. in the total cases. The percentage of relapses in the bacilluria cases was 36 per cent., against 20 per cent. in the total series.

Character of the Eruption. The bacilluria appears to be independent of the eruption of typhoid fever. In some few cases of recent observers, the two have been coincident, both no doubt indicating the distribution of minute septic emboli. In general, the majority of observers agree that the infection of the urine occurs more frequently in those cases which have borne a well-marked eruption. In my series of 50 cases, 11 bore a well-marked eruption, 12 a moderate, and 20 a scanty eruption; and in 7 cases no spots were observed. In the bacilluria cases, the eruption in 3 was well marked, in 7 moderate, and in 1 scanty.

Albuminuria. Albuminuria is frequently co-existent with typhoid bacilluria. Its relation to the presence of the bacilli has been the subject of discussion, based on diverse findings of individual investigators. That a closely dependent relation exists, such as was insisted upon by Bouchard and Seitz, and later by Besson and Schichhold (that is, without albuminuria, no bacilluria), is refuted by the observations of the majority of investigators. True, the greater number of all cases of bacilluria reported have shown a co-existent albuminuria, and in a small number of these cases the

two conditions have been synchronous in onset, in duration, and in disappearance. On the other hand, the majority of urines which contain albumin, coming usually in high febrile stages, show no bacilli.

The typhoid bacilli have appeared in the urine in fully one-third of all cases that contain no detectable albumin; they have appeared in the urine in many instances in which at no stage of the disease has albumin been observed (Brown, 4 out of 8 cases; Vincent, 2 out of 9; Vas, 2 of 4; Lesieur and Marchand, 3 of 10); and finally, they have disappeared spontaneously from urine which continued to contain albumin, and have persisted in urine from which the albumin had vanished (cases of Brown, Vas, Richardson, Horton Smith, and others). Therefore albuminuria is not a necessary factor in the establishment of typhoid bacilli in the urine. Albumin, if present, improves the urine as a culture medium, as has been shown, and presumably its presence indicates a more or less incompetent condition of the kidney.

Of my 50 cases, 35 had albuminuria at some period, usually the high febrile stage, a ratio to the total of 70 per cent. Of the 11 bacilluria cases, 7 showed at some stage serum albumin, varying from a very faint trace up to 0.1 per cent., a ratio of 64 per cent. Of these 7 cases, 5 showed albumin at sometime when the bacilli were also present. In one case the bacilluria came on simultaneously with albuminuria. In 2 cases the albumin disappeared before the bacteria. In 1 case albumin persisted after the bacilli had spontaneously disappeared. Care was taken to avoid confusing pus with serum albumin.

Clinical Course of Bacilluria. 1. *Symptoms.* As a rule, typhoid bacilluria gives no suggestive symptoms; even when the urine contains a heavy sediment of pus in addition to the swarming bacteria, the patient rarely complains of frequency, burning, or tenesmus. Infection of the urine with organisms other than the typhoid bacillus is by no means rare in typhoid fever. In these cases symptoms are often present. But to the typhoid organism itself the bladder seems very tolerant, possibly because this bacterium in its growth does not markedly alter the reaction of the urine, nor tend usually to invade the bladder wall.

Objectively, the urine is often turbid from the enormous number of bacilli. This is the rule in the bacillurias occurring during convalescence. Horton Smith noted turbid urine in 23 out of 26 typhoid bacilluria cases; others observed it less frequently, Shuder even finding no turbidity. Eight of my cases showed turbidity at some period of the bacilluria. The degree of turbidity varied much in the given case from day to day, the urine usually clearing macroscopically some days before it was sterile on culture.

A shimmer on swirling the urine in a test-tube has been described. This is due to the reflection of light from the different planes of

moving bacteria, but it is not characteristic of the typhoid organism alone, occurring in any bacilluria, unless obscured by pus or precipitate. Pus, usually in small quantity, is present in the majority of those cases showing turbidity. In how far this condition, in the absence of subjective symptoms and in consideration of its ephemeral character, may be dignified by the term cystitis, is a matter for individual determination.

2. *Complications.* The cases of true cystitis due to the typhoid organism alone, with sharp subjective symptoms and pathological changes in the bladder wall are exceptional. Acute cystitis or pyelitis appearing during the course of typhoid fever is usually due to some other organism. Vincent, in 1200 cases of typhoid fever, noted only two cases of acute cystitis due to the typhoid organism, coming on in convalescence. In rare instances the typhoid bacillus produces ulcerative lesions simulating those produced by the tubercle bacillus. Rousig observed an acute cystitis for two months, until the death of the patient, which was caused by the typhoid bacillus alone. This case on cystoscopy showed deep ulceration of the bladder. Brown reported a case with like bacteriological and cystoscopic findings, apparently arising from using an infected catheter. Houston reported a case of severe typhoid cystitis. It is of interest to note that the only tangible source of the urine infection in this case was by exposure while nursing a case of typhoid fever three years previously. Young reported a case in which the cystitis had been of five years' duration, following an attack of typhoid fever. The man had a history of previous venereal and prostatic disease. Cultures showed considerable numbers of typhoid bacilli accompanied for a time by the gonococcus. The bladder retained 16 ounces of residual urine, and on cystoscopy showed chronic ulcerations. This case was treated unavailingly for two years, when the man disappeared.

A patient with pyonephrosis recently operated upon at the New York Hospital by Dr. F. W. Murray contained the typhoid organism in pure culture. The infection probably dated from an attack of typhoid fever five years previously. The man was also supposed to have had an attack of typhoid fever eighteen years previously.

In that unusual invasion of typhoid fever, such as the nephrotyphoid case reported by Napier and Buchanan, in which the kidney rather than the intestine is the prominent organ of initial bacterial attack, the bacilluria is probably secondary to the renal invasion.

3. *Termination.* Why typhoid bacilli once established in the urine should disappear spontaneously is a difficult question to answer with accuracy. Yet the answer is of importance, not only on theoretical grounds, but also from the standpoint of actual practice. General body resistance is probably no factor in the dis-

appearance of the microörganism. The termination bears no relation to the appearance or intensity of the agglutinating power of the blood serum, if we may take the agglutinins as an approximate index of the bacteriolysins. The bacteria appear and disappear in the early stages of typhoid fever, before the serum reaction has appeared; they appear and disappear in the afebrile stage when resistive powers have fully developed. Phagocytosis evidently plays no part, for the leukocytes of the urine do not contain noteworthy numbers of bacilli, and the bacteria disappear from urine which contains no excess of leukocytes.

Agglutinins and antitoxins in the urine play no proved part. Certain investigators have found that minute quantities of various agglutinins do come through the kidney. This has not been satisfactorily proved of typhoid. Although the bacilli appearing in the urine in typhoid fever do tend to be stunted and have lost in whole or in part the active motility seen in bouillon culture, yet in my experience the same phenomenon is observed if typhoid bacilli are planted in normal urine of equal acidity. Vincent reported the feeble agglutination of typhoid bacilli in the urine from a case fourteen days ill, and from another of thirty-seven days. In eight cases I could not confirm this observation. Actively motile bacilli were placed in the urines of 8 febrile and convalescent typhoid fever patients who gave in the blood serum intense agglutination. In none at the end of twelve hours could any more clumping or cessation of motion be observed than in normal urines of like acidity.

Bacteriolytic action does not explain the disappearance, for the urines from which the bacteria have disappeared spontaneously sometimes continue favorable media for typhoid growth. Four such urines were planted in vitro. In one the bacilli developed luxuriantly, in the other three scantily. Mechanical outwash alone does not explain the disappearance, for frequently the bacteria first appear or markedly increase during the stage of polyuria, when the outwash is great.

The most satisfactory explanation is that the bacteria, usually finding no foothold other than the bladder urine, come upon a period when the urine is a poor medium; growth is inhibited, but the outflow is continued. Thus gradually the last bacterium is washed from the bladder.

On this hypothesis the factors favoring cure are, first, any condition that acidifies the urine or otherwise makes it a poor medium, such as fever, increased metabolism, or diminished water ingestion; second, any factor increasing the expulsive power of the bladder, such as upright posture and improved general muscular tone. Occasionally, in spite of one or the other of these factors, the bacteriuria continues. In these cases it has usually been noted that some unusually favorable feature was present; as, for instance, in

Jacobi's cases, in which, in spite of high temperature, the bacilluria continued, it is presumable that the accompanying nephritis and hematuria repeatedly re-infected the urine; and, again, in such cases as Young's and Houston's, persisting over years in spite of the upright posture, not only the urine but also the bladder wall has been found to be infected. In the absence of any actual tissue infection, it must be assumed in accounting for such cases as Rousig's, lasting over periods of months, that either the urine remained a good medium over this period or that the bacilli were harbored in some unusual way, as, for instance, in residual urine, this latter apparently accounting for a persistent case of my own.

Of five personal cases which cleared up spontaneously, the bacteria disappeared in four, presumably from the causes stated. In the fifth case the typhoid organisms were overgrown by newly implanted, more vigorous bacteria. In this case the urine showed typhoid bacilli in pure culture on the twenty-second and twenty-sixth days. Then on account of retention the patient was repeatedly catheterized. Cystitis developed and cultures on the twenty-eighth day showed colon bacilli as well as typhoid. On the thirty-first day the urine had become ammoniacal and cultures showed only colon and proteus, no typhoid bacilli.

Virulence of Typhoid Bacilli in the Urine. Horton Smith found the typhoid organism occurring in the urine to be as toxic to animals as the one from the feces or blood. There is no direct proof of its pathogenesis in man by the Koch cycle. The nearest approach to the cycle is a case related by Sheele, of a servant who in misapprehension drank from a flask in which some urine had been secreted by a typhoid fever patient. She herself developed typhoid fever twelve days later. There is no reason to doubt the virulence of these organisms. Morphologically, culturally, biochemically, and in so far as the serum reactions are concerned, these organisms do not differ from the organisms obtained from the blood or the stool.

Diagnostic Value of Typhoid Bacilli in the Urine. As an aid to diagnosis in the average case of typhoid fever, bacterial search of the urine is of minor importance. The condition usually occurs late in the disease and in a relatively small number of cases as compared with the blood infection, and the technical difficulties surrounding clean catheterization, particularly in women, are greater than with the serum reaction or the blood culture. In five cases in which the blood was observed as well as the urine, Lesieur and Marchand found the appearance of the bacilli in the urine to be uniformly later than their appearance in the blood.

However, in the atypical and irregular cases urine cultures are frequently of great diagnostic value. Particularly in the renal type of typhoid invasion, and in the overwhelming septicemic types, it is of value, often being the earliest means of exact diagnosis in

such cases. Revillard observed a patient who presented the symptoms of a unilateral septic kidney, while a case of Singer simulated a meningitis of mastoid origin; in both the correct diagnosis was reached by culture of the urine, and Napier and Buchanan reported a case at first diagnosticated as idiopathic acute nephritis.

In one case only of my eleven, did the finding of the bacillus antedate a positive Widal reaction. In this the bacterium was found on the seventeenth day; the serum agglutination did not appear until the fifty-second day, during a relapse.

Typhoid Bacilluria a Public Menace. To the patient the condition is usually not a menace. Complications are unusual; the bladder tolerates the presence of the organism; the resistive forces are such that general re-infection is improbable. But to the non-immune public the condition is a real menace. Indeed, the urine may well be considered the most dangerous of all excreta.

The dearth of subjective symptoms makes the condition one that is easily overlooked. Nor are the objective signs of obtrusive prominence. The stool, not the urine, has borne the brunt of popular condemnation and prophylaxis, for the stool is offensive physically; it is closely associated in the public mind with the notion of typhoid fever as a strictly enteric condition. The soiling of bath and linen by fecal matter is evident and quickly cared for; the stool is guarded more carefully from the fly, and is crowded through to disinfection with greater celerity.

Furthermore, as against fecal dissemination, the stool contains its maximum number of typhoid organisms only at the height of the illness, when the patient is under the closest observation. In the latter stages, when control over the patient is being relaxed, the typhoid organisms have usually disappeared from the intestine; the ulcers which sowed the feces have healed; the typhoid bacilli free in the intestine have been overrun by the more vigorous colon, proteus, and other saprophytic organisms; and, unless the bile has become infected, the bacilli have ceased in the stools. Herbert, in 216 examinations of stools in 98 cases of convalescent typhoid fever patients, found the organism in the stool in only 3 cases. In the urine of these 98, he found the bacilli in 18 cases.

Although with the newer media, such as the Conradi-Drigalski, the organism can be recovered in practically every case by a persistent search in the feces of the active typhoid fever case, and although against this can be set only 24 per cent. of cases in which the urine has been proved to be infected, yet considering the stage at which the bacteria appear in the urine, the period of duration of the bacilluria, the greater likelihood of carelessness with the urine, the overwhelming numbers in which the bacteria appear, and the frequency and promiscuousness of urination as compared with defecation, the conclusion is inevitable that the urine of typhoid

fever is the great spreader of this disease. Such is the opinion of Horton Smith, Knox, Lesieur, and many other competent judges.

There can be no question that the urine of the immediate post-typhoid patient is a serious menace to the community, far outweighing the dangers of fecal dissemination. But when it comes to periods long after typhoid fever and to the consideration of those cases which years after their attacks of typhoid fever carry virulent organisms in their bodies, and continue to infect their fellowmen, such cases of typhoid bacilli carriers as have been run to earth by Liebetrau, Kayser, Soper, and many others, the urine is found far less frequently at fault than the feces. This is as one might assume in considering the urine as a medium in which the growth of the organisms is frequently inhibited by high acidity, as against the bile in which, as shown by Conradi, typhoid bacilli flourish at all times, especially according to Foerster when slightly albuminized by inflammatory exudates.

With the active menace of this condition of bacilluria in view, it must become a rule so to treat every case of typhoid fever as to avoid danger of urinary dissemination of the disease.

Treatment of Typhoid Bacilluria. The condition demands treatment chiefly from the standpoint of public health. From the patient's standpoint, drastic remedial measures are unjustifiable, and those used must be the mildest that can adequately cope with the situation. The urine in all stages of typhoid fever must be regarded as highly infectious, and subjected to the same thermal or chemical disinfection as the feces. During that stage in which the condition of enduring bacilluria usually makes its appearance, the urine in the bladder should in every case be rendered unfit for the growth and maintenance of typhoid organisms.

Richardson first in any extensive work called attention to the value of urotropin (hexamethylenamin) as a cure for this condition. He treated nine cases successfully. In several cases the bacilluria was terminated within two days, in all within two weeks. Eight were completely cured by a total of sixty grains of the drug. Horton Smith cites at length 10 cases, and remarks on the marvellous transition in each case from a turbid, oftentimes pus-ridden urine, to a clear urine within a single day, under the administration of this drug. Three cases were cured by ten grains three times a day, in one day, the most obstinate within twelve days. Gwyn of all the observers has met with least success with urotropin. Of three cases, he was successful in one after a total of 165 grains. In another he observed an increase in the number of bacilli during treatment. In the remaining five of his eight cases he resorted to bichloride of mercury, 1 to 50,000 as an irrigation, succeeding in three cases. Brown, Jacobi, and others, have been successful with urotropin. In many instances, however, on the cessation of the drug after administration for two or three days, and in some cases longer, the bacilli reappeared a few days after medication was suspended.

In four carefully followed cases of turbid typhoidal bacilluria, three with a moderate amount of pus, I administered urotropin, five grains, three times a day. The urine became clear within twenty-four hours, and the bacteria disappeared in three cases within seventy-two hours, but in one case they persisted in small numbers up to the eighth day.

To determine if there were active bactericidal property to urotropin urine, three urines from which the bacilli had promptly disappeared under urotropin were planted with a bouillon culture of typhoid. Living bacilli were recovered in each case at the end of twenty-four hours. Inhibitory action, however, was evident, because no increase in the bacilli planted took place. To determine how great was the inhibition, these three specimens were mixed with bouillon in the proportion of 10, 25, and 50 per cent., and inoculated. One urine absolutely inhibited in all dilutions, one in the 25 and 50 per cent. mixtures, and one in the 50 per cent. mixture only. In other specimens from five patients receiving urotropin, 5 grains three times a day, the bacilli uniformly failed to grow in the undiluted urine, and also in the urine diluted 50 per cent. with bouillon. In four of the undiluted specimens the bacteria were still living at the end of a week. In one specimen they had died out. Urotropin, then, while having but slight bactericidal power over typhoid bacilli, is markedly inhibitory. This inhibition persists in the urine for from one to two days after the suspension of medication.

The disappearance of the bacteria from the patient's urine under urotropin seems due not to a positive bactericidal action, but to an inhibition of growth which finally allows the last bacterium to be washed out mechanically. In the majority of cases reported by various observers this inhibition of growth and elimination has been completed within three days. However, cases are not uncommon, though in the minority, in which recurrence of the bacilluria has taken place, on the suspension of the drug, at the end of one to three days. In rare cases, even a two weeks' course of treatment has not sufficed to eradicate the organisms.

It is evident, by the ease with which the bacteria are vanquished, that usually the urine alone, not the bladder wall, is infected. The cases of ulcerative cystitis, which fortunately are rare, would seem not amenable to urotropin, no matter how long continued. Such, in fact, was the observation in Young's case, in which long-continued usage of urotropin combined with antiseptic irrigation was unsuccessful in eliminating the organisms. Antiseptic irrigation or surgical drainage would offer the best hope of cure in these cases.

Long-continued administration of urotropin in full doses is to be condemned. In overdose and in susceptible patients the drug is capable of much harm. It is not uncommon to see it produce tenesmus, blood in the urine, and, rarely, even hemorrhagic nephritis. Prudence, therefore, dictates the minimum effectual quantity, and

for the minimum effectual length of time. The limits of such administration remain for future determination, and, indeed, a more acceptable medication may be found. Such is suggested in benzoic acid by the work of Winslow and Lochridge. They have found this almost as toxic to typhoid bacilli as the mineral acids, killing in n/200 in forty minutes. Both benzoic acid and its derivative, hippuric acid, are unfavorable to typhoid growth in the urine.

For a routine procedure, Shattuck advises urotropin, ten grains three times a day, twice a week during and after typhoid fever. At the New York Hospital the usual routine of late has been 15 to 30 grains a day, for the week preceding and the two weeks subsequent to normal temperature. Complaints of vesical tenesmus under such administration have not been infrequent (in 4 out of 14 consecutive cases in which I inquired), but in none was there hematuria.

The problem is to secure the maximum inhibitory and curative effect of the drug with the minimal dosage. Since the first 20 grains usually suffice to clear the urine macroscopically, and the continuance of administration of 20 to 30 grains for three days has in a large majority of cases permanently freed the urine from bacilli, the following would seem to be a reasonable rule in the routine treatment of typhoid fever as a prophylactic measure: From the time when the fever approaches normal, and continuing four weeks into the convalescence, every typhoid fever patient should receive half a gram of hexamethylenamin three times a day for three consecutive days of each week. If bacilluria becomes established, it should be treated by the administration of the drug for continuous periods of a week. Failing thus to eradicate the organism, the bladder should be washed out daily with silver nitrate solution, 1 to 5000, or other antiseptic. Chronic ulcerative cases should be drained by cystotomy.

SUMMARY. The facts concerning typhoid bacilluria should be more widely known, and the responsibility of its prevention appreciated.

1. Typhoid bacilli are present in the urine of at least 24 per cent. of all cases of typhoid fever.

2. They are usually found in enormous numbers, appearing at about the time that the temperature falls to normal; and they continue in varying intensity, sometimes intermittently usually for several weeks, tending to disappear spontaneously.

3. The bacilluria arises from infection of the bladder urine from the blood, probably by way of the kidney.

4. Typhoid organisms multiply most rapidly in urine of low acidity. Highly acid urine is inhibitory principally because of the organic acidity. The urine at the height of the fever is usually highly acid and a poor medium; that of the declining stage is low in acid and a good medium for the growth of typhoid bacilli.

5. Atony and overdistention of the bladder and the presence of residual urine are occasionally factors in permitting the typhoid bacillus to become established in the bladder urine.

6. Severe cases of typhoid fever are more subject to infection of the urine than milder cases.

7. The eruption bears no consistent relation to the bacilluria.

8. Albuminuria is not essential to the establishment of the bacilli in the urine. Albumin, however, enriches the urine as a culture medium and indicates such renal damage as might more readily allow the passage of bacteria from the blood.

9. Absence of subjective symptoms is the rule. Objective signs are usually present at some period of the infection; such signs as slight or moderate turbidity of the urine, a shimmer on swirling in a test-tube, or the presence of a small amount of pus. The only dependable sign is the presence of the bacillus proved by culture from the catheterized or cleanly passed urine.

10. Complications are rare. True cystitis occurring during typhoid fever is usually due to some organism other than the typhoid bacillus. Acute typhoid cystitis does occur; and a few cases of pure typhoid infection causing a chronic ulcerative cystitis are recorded, as also are chronic infections of the kidney.

11. The bacilli usually disappear spontaneously. The eliminative agents seem to be, first, an inhibition of growth due to an increased acidity of the urine in the stage of active convalescence, and second, increased power and completeness of urination.

12. The typhoid organism in the urine is virulent.

13. For diagnosis in a case of suspected typhoid fever bacteriological examination of the urine is rarely of value.

CONCLUSIONS. 1. Typhoid bacilluria is a great menace to public health. Of all excretions containing typhoid bacilli, the most dangerous is the urine of the declining and postfebrile stage of typhoid fever. The feces are a greater public menace during the active stage of the illness, but taking the course of typhoid fever as a whole, the urine is probably the great spreader of this disease. However, in chronic typhoid-bacillus carriers, the bile more frequently than the urine is the medium in which the bacteria have perpetuated themselves.

2. As a routine in every case of typhoid fever, during the decline and convalescence, the urine in the bladder should be rendered inhibitory to the growth of typhoid bacilli. Bacilluria once established should be terminated by urinary antiseptics or by irrigation of the bladder. Obstinate ulcerative cystitis should be treated by surgical drainage. The passed urine of the typhoid fever patient at all stages of the illness should be disinfected with the same care as the feces.

BIBLIOGRAPHY.

Abe. Münch. med. Woch., 1907, 1924.
Baarte de la Faille. Cent. f. Bakt., 1895, xviii, 337.
Besson. Rev. de méd., 1897, xvii, 405.
Bliss. Edin. Med. Jour., 1902, xii, 337.
Blumer. Johns Hopkins Hosp. Rep., 1895, v. 327.
Borges. Durchlassigkeit der Typhus-niere, Inaug. Diss., Wurzburg, 1894.
Bouchard. Rev. de méd., 1881, i, 671.
Brown. Edin. Med. Jour., 1905, xix, 116.
Brown. Medical Record, 1900, lvii, 405.
Büsing. Deut. med. Woch., 1902, 443.
Coleman and Buxton. Amer. Jour. Med. Sci., 1907, cxxxiii, 896.
Curschmann. Münch. med. Woch., 1900, 1449.
Drigalski. Cent. f. Bakt., I Abt. Orig., 1904, xxxv, 776.
Eberth. Virchow's Archiv, 1880, lxxxi, lxxxiii.
Englisch. Wien. med. Presse, 1907, xlviii, 1126.
Flamini. Riv. di clin. ped., 1903, i, 97.
Flexner. Jour. Path. and Bact., 1896, iii, 202.
Folin. Amer. Jour. Phys., 1903, ix, 265.
Fuchs. Wien. klin. Woch., 1902, 170.
Geisler. Cent. f. Bakt., 1893, xiii, 767.
Gwyn. Johns Hopkins Hosp. Bull., 1899, x, 109; Johns Hopkins Hosp. Rep., 1900, viii, 389.
Herbert. Münch. med. Woch., 1904, 472.
Horton Smith. Med.-Chir. Trans., 1897, xviii; Lancet, 1899, i, 1349; 1900, i, 830, 915, 1059.
Houston. Brit. Med. Jour., 1899, i, 79.
Hueppe. Fortschr. d. Medicin, 1886, iv, 416.
Jacobi. Deut. Arch. f. klin. Med., 1902, lxxii, 442.
Kayser. Ztschr. f. Med., 1906, xix, 176.
Karlinski. Prag. med. Woch., 1890, xv, 437, 452.
Klimenko. Arch. Russes d. path. d. med. clin., 1901, xii, 141.
Knox. Jour. Royal Army Med. Corps, 1904, iii, 1.
Konjajeff. Ref. Cent. f. Bakt., 1889, vi, 672.
Liebetrau. Arbeit. a. d. Kaiser. Gesundheitsamte, 1906, xxiv, 341.
Lesieur. Hygiène gén. et appliq., Paris, 1906, i, 546.
Lesieur and Mahaut. Med. Klinik, 1905, 929.
Levy and Gissler. Münch. med. Woch., 1897, 1435.
Lewis. Edin. Med. Jour., 1901, x, 261.
Merkel and Goldschmidt. Cent. f. klin. Med., 1887, 12.
Munch. Sem. méd., 1904, xxiv, 121.
Napier and Buchanan. Glasgow Med. Jour., 1906, lxvi, 401.
Neufeld. Deut. med. Woch., 1900, 824.
Neumann. Berl. klin. Woch., 1887, vii, ix; 1890, 121.
Park. Trans. Assoc. Amer. Phys., 1901, xvi, 634.
Paus. Cent. f. Bakt., I Abt. Orig., 1907, xlv, 81.
Petruschky. Cent. f. Bakt., 1898, xxiii, 577.
Remlinger. Presse méd., 1907, xv, 35.
Revilliod. Ref. Virch. Jahresb., 1896, ii, 12.
Richardson. Jour. Exper. Med., 1898, ii, 349; 1899, iv, 19; Boston Med. and Surg. Jour., 1903, cxlviii, 152.
Rousig. Infect.-Krankheit. der Harnorgans, Berlin, 1898.
Sato. Saitake Gaku Zasshi, Tokyo, 1903, xc, I.
Schichhold. Deut. Arch. f. klin. Med., 1899, lxiv, 505.
Seitz. Bact. Studien sur Typhus Aetiologie, Munich, 1886.
Shattuck. New York Med. Jour., 1904, lxxx, 329.
Shuder. Deut. med. Woch., 1901, xxvii, 763.
Shumberg. Deut. med. Woch., 1901, ix, 134.
Silvestrini. Riv. Gen. Ital. d. Clin. Med., iv, 1892.
Simon and Dennemark. Deut. Militar. Zeit., 1907, xxxvi, 86.
Singer. Orv. Hetiszemle, 1896, xxi.
Vas. Wien. klin. Woch., 1906, xix, 368.
Vincent. Seances de la soc. de biologie, 1901, liii, 275; 1903, lv, 365.
Winslow and Lochridge. Jour. Infec. Dis., 1906, iii, 547.
Wright and Semple. Lancet, 1895, ii, 196.
Wyssokowitsch. Ztschr. f. Hygiene, 1886, i, 3.
Young. Johns Hopkins Hosp. Rep., 1900, viii, 401.

THE SURGICAL TREATMENT OF PERFORATION OF THE INTESTINES IN TYPHOID FEVER.[1]

A REVIEW OF THE LITERATURE.

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of Philadelphia.

The importance of perforation of the intestine in typhoid fever can be best indicated by a brief review of the prevalence of typhoid fever in general, and the report of 369 cases of perforation of the intestine gathered from literature since the classical paper by Harte and Ashhurst,[2] in which they record 362 cases, with 268 deaths, an operative mortality of 74.03 per cent.

Frequency of Typhoid Fever. The reports of the United States Census Bureau show that in the "Registration Area" for the years 1901 to 1905 inclusive, there was an average per year of 10,458 deaths from typhoid fever, or a mortality rate of 32.2 per 100,000 of population. In 1906 this jumped to 13,160 deaths, the increase being due, in part, to an enlargement in the size of the registration area and also to a higher mortality of the disease in that year. The mortality of typhoid fever in this country is only exceeded by that in Finland, Ceylon, Servia, Australia, Spain, and Italy. In the registration area the highest death rate is found in Pennsylvania, with a mortality rate of 56.5 per 100,000 of population.[3] To all these figures the city of Philadephia has contributed more than one would expect, for from January 1, 1903, to September 15, 1908, there have occurred 32,218 cases, with 4930 deaths.[4]

Frequency of Perforation. Vaughan[5] states that the frequency of perforation has been variously estimated at from 1.3 to 2 per cent. Of necessity, the statistics vary in different epidemics of the disease. Edsall[6] has observed that hemorrhage and perforation have a tendency to occur in groups in hospital practice, and he believes it to be a question whether or not complications or severe abdominal symptoms are not due to some secondary infection rather than to the typhoid infection itself. I have collected 21,215 cases of typhoid fever from literature; perforation occurred in 671, a frequency of 3.16 per cent.

Etiology of Perforation. The causes of perforation may be classified as predisposing and exciting. Among the former is sex,

[1] Read in abstract at the meeting of the Philadelphia County Medical Society, October 28, 1908.

[2] Annals of Surgery, January, 1904.

[3] Report of the Commissioner of Health, Pennsylvania, 1905–1906.

[4] Personal communication from the Director of the Department of Health and Charities, Philadelphia.

[5] Washington Medical Annals, March, 1906. [6] Amer. Jour. Med. Sci., April, 1908.

with the greatest frequency in males. My analysis comprises 281 males and 58 females; in 30 cases the sex is not stated. This preponderance of the male sex is of necessity an incidence of their greater liability to the disease. So, too, age is a factor, the larger number of cases occurring before the age of thirty years. In this analysis 249 cases were under thirty-one; in 75 cases the age was over thirty-one; and in 45 cases it was not stated. Kisberg[7] quotes Henoch, Baginsky, Morse, and others as stating that perforation is rare in children, a statement which, as Elsburg has shown, is not substantiated by a study of the reported cases. Elsberg notes 25 cases, and I have collected 68 additional cases, all of which were subjected to operation. That children stand operative interference better than adults is well shown by the fact that of these 68 cases only 31 died, a mortality rate of 45.58 per cent. Intestinal parasites may be either a predisposing or exciting cause, or both. Tympany may be a factor in the production of perforation; as Curschmann[8] points out, when excessive it causes paralysis of the muscular layer of the intestine and consequent immobility.

The exciting causes of perforation are, as a rule, mechanical, and anything that causes a sudden or unusual stimulation of peristalsis must be regarded as a possible etiological factor.

Time of Perforation. While statistics show that more than 70 per cent. of the cases of perforation occur between the second and fifth week of the disease (in 413 out of a series of 568 cases it occurred during that time), still it should be remembered that perforation may occur at any time during the course of the disease, in a relapse, or even in convalescence. In Goodall's[9] series of 96 cases, in 9.3 per cent. the perforation took place during a relapse. Briddon[10] has noted a perforation occurring on the twelfth day of convalescence, and Panton[11] another on the twenty-seventh day. Pluyette and Allezars[12] report a case of typical typhoid perforation of the ileum occurring two months after the cessation of the fever and unaccompanied by any symptoms of a relapse. So, too, perforation may occur in the ambulatory case as well as in the one in which the severity of the symptoms is marked, but more commonly it occurs in the latter.

Pathology. The pathology of the intestinal lesions of typhoid fever is so well known that it seems unnecessary again to consider it in detail, save to emphasize the fact that the lesions are, as a rule, situated on the free border of the intestine opposite the mesenteric attachment; thus, at a point where the blood supply is relatively poor, and which in itself predisposes to necrosis and subsequent perforation, As Maylard[13] has stated, the tendency of the typhoid

[7] Annals of Surgery, July, 1903.
[8] Nothnagel's Encyclopedia, American edition, 1907.
[9] Lancet, 1904, ii, 9.
[10] Annals of Surgery, 1896, xxiii, 198.
[11] Ibid., 1897, xxvi, 219.
[12] Marseille méd., 1904, xli, 321.
[13] Surgery of the Alimentary Canal, London, 1900, p. 247.

ulcer is to perforate in contradistinction to the ulceration of tuberculosis. It is rare that perforation takes place into the mesentery with the formation of a retroperitoneal abscess; most common is perforation into the general peritoneal cavity. Numerous observers have called attention to the fact that there is but slight tendency to the formation of adhesions and consequent localized abscess; a few such cases have been observed by Da Costa,[14] Holmes,[15] and others.

ANATOMICAL LOCATION. While the ileum is the most common seat of the perforation, no portion of the gastro-intestinal tract, except the duodenum, is apparently exempt.

Stomach. Mauger[16] quotes Milliard as reporting 2 cases and Louis 1 case of perforation of this viscus. Basile[17] reports the case of a woman, age not stated, on whom at operation he found the perforation of a typical typhoidal ulceration of the posterior surface of the stomach. Mazetti[18] states that at autopsy on a patient who died of typhoid fever, he found a perforation of the posterior wall of the stomach near the pylorus.

Jejunum. Beros[19] reports 2 cases: 1 discovered at operation and the other at autopsy.

Ileum. In my study of 369 cases the ileum was the seat of perforation in 279, or in 75.60 per cent. of the cases.

Meckel's Diverticulum. Mauger notes the cases reported by Golton, Dreyfus, Delanglade, and also a personal communication from Heurteaux reporting the successful operation in a boy aged ten years. Long[20] also notes another successful case in a man aged twenty-five years. Goodall observed one case postmortem and Landis[21] another similar case.

Cecum. Mauger notes the 8 cases reported by Leudet (3 cases), Rokitansky (2 cases), Milliard, Thompson, Herbert and Thurston. In my statistics are included 5 subsequent cases reported by: Boussenot,[22] male, aged twenty-two years; operation, death; Claybrook,[23] male, aged eight years, operation, recovery; Fontoynont,[24] male, aged twenty-two years, operation, death; Scott,[25] female, aged twenty-two years, operation, recovery; Haggard,[26] male, aged twenty-three years, operation, death.

The Vermiform Appendix. The limitation of the space at my disposal does not permit of a detailed consideration of the appendi-

[14] Personal communication.
[15] Jour. Amer. Med. Assoc., March 14, 1903.
[16] La perforation typhique de l'intestin et de ses annexes, son traitement chirurgical, Thèse de Paris, 1900.
[17] Il Policlin., 1905, tome xx, ses Prat., p. 157. [18] La Riforma med., 1908, xxiv, 487.
[19] Contributions a l'etude des perforations intestinales chez les typhiques, Thèse de Bordeaux, 1906–1907.
[20] Surgery, Gynecology, and Obstetrics, 1907, iv, 301.
[21] Personal communication. [22] Bull. méd., 1905, xix, 109.
[23] Personal communication.
[24] Bull. et mém. soc. de chir. de Paris, 1908, xxxiv, 701.
[25] Personal communication. [26] Personal communication.

ceal complications of typhoid fever, which have been admirably described by Deaver,[27] Francois,[28] Frazier and Thomas,[29] Hopfenhausen,[30] Rolleston,[31] and others. Briefly stated, it may be said that the appendix during typhoid fever may be the seat of any possible grade of inflammation, and that this may terminate in resolution or in the surgical calamities of perforation or pus formation. Deaver collected 40 cases of perforation, of which 7 were operated upon, with 4 deaths; the remaining 33 all died. I have collected 15 additional cases, all of which were operated upon, with 5 deaths—a mortality of 33.33 per cent. Deaver notes 41 cases of inflammation, of which 30 were subjected to operation, with 4 deaths; of the 10 cases not operated upon, 9 died. I have collected 22 additional cases, all of which were operated upon, with 4 deaths—a mortality of 18.18 per cent. In practically all of the inflammatory cases that recovered the operation was performed early in the disease. I agree with Deaver that during the height of the disease it is best not to operate, unless there is good evidence of perforation or pus formation.

Colon. Prevost-Maisonnay[32] reports 2 cases, and in my analysis are included 12 subsequent cases.

Rectum. Mauger states that Leudet and Hutinel have each reported cases in which the rectum was the seat of a perforation. In 57 cases the anatomical location of the perforation was not stated.

Size and Number of Perforations. The size of the hole in the intestine may vary from that of a pin point to that of a fifty cent piece, or larger. As a rule there is only one perforation, but there may be more. Scott[33] reports a case in which there were five, and in my study the perforations were multiple in 31 of the cases. As Selby[34] has emphasized, the leakage of the intestinal contents is of necessity in direct proportion to the size of the perforation.

Symptoms. The symptoms of perforation should be divided into two classes: those occurring immediately at the time of perforation, and those later symptoms which are the result of it, or, in other words, those of the succeeding general peritonitis.

The symptoms of actual perforation may be either abrupt or gradual in their onset, and in a certain small number of the cases all leading symptoms are conspicuous by their absence. More commonly the onset is abrupt, and McPhedran[35] has observed that

[27] Appendicitis, etc., Philadelphia, 1905.
[28] L'appendicite au cours de la fievre typhoide, Paris, 1904.
[29] Univ. Penn. Med. Bull., July–August, 1907.
[30] Rev. med. de la suisse romande, 1899, xix, 105.
[31] Lancet, May 29, 1898.
[32] Lesions du colon dans la fievre typhoide, Thèse de Paris, 1899.
[33] Univ. Penn. Med. Bull., 1905, xviii, 81.
[34] Amer. Jour. Med. Sci., 1908, cxxxv, 224.
[35] Canada Lancet, March, 1907.

the symptoms of perforation vary according to the situation which the perforated bowel occupies in the abdominal cavity—the nearer it lies to the centre of the abdomen the more fulminating will be the local and constitutional symptoms. It should be remembered that there is no pathognomonic symptom of perforation.

Martin[36] and McCrae[37] have each noted that while more or less abdominal pain may be present in the course of typhoid fever, the onset of sudden abdominal pain is a symptom of perforation of the first importance. As Manges[38] aptly states: "It is the constancy of the early occurrence of pain which makes it so important as a symptom of perforation." This pain varies in intensity and location; it is usually more or less localized to the lower right quadrant of the abdomen, or it may be referred to the umbilicus. As a rule it is a constant pain, becoming more intense at intervals. Pain that is localized at first but later becomes general throughout the abdomen, is an indication of a progressive general peritonitis. In cases of severe infection the apathetic, delirious, or comatose condition of the patient may entirely mask this subjective symptom, which, however, is prominent in fully three-quarters of the cases.

What has been described as the sudden classical fall of temperature in the light of our further knowledge, seems to be the exception rather than the rule. Scott states that a sudden rise of 1° or 2° followed by a slow but persistent fall to normal or subnormal over a period of eight to ten hours is more common, but in some few cases there is no appreciable change. The pulse rate usually rises rapidly; one of 140 beats per minute is not uncommon within twenty minutes after the time of perforation.

The two physical signs of the utmost importance that are usually present are tenderness and rigidity. The tenderness may be most marked at the point of pain, and this is accompanied by rigidity, usually more marked on the right than the left side in the beginning; with the onset of general peritonitis it is found in all the abdominal muscles.

So, too, the facial expression undergoes a change difficult of description; it is what the French have appropriately termed an "abattement," or weakening of the countenance, which, with the onset of general peritonitis, is replaced by the facies so characteristic of that disease.

Percussion of the abdomen may or may not aid in the diagnosis, for the normal liver dulness may have been obliterated previously by reason of intestinal distention. Manges, with an experience of 19 cases, states as his belief that it may be a sign of value if care be taken to watch daily any alteration in it.

[36] De la douleur abdominale dans la fievre typhoide, Thèse de Paris, 1901.
[37] New York Med. Jour., May 4, 1901.
[38] Jour. Amer. Med. Assoc., April 1, 1905.

The knowledge to be gained by an examination of the blood is as yet still a disputed point, save that as, Shattuck, Warren, and Cobb[39] have emphasized, an isolated count is valueless. Thayer[40] first showed the hypoleukocytosis of this disease, and Scott quotes Kast and Gutig, and Le Conte and Lewis as having drawn attention to the fact that in typhoid fever the onset of complications is not characterized by a leukocytosis. Differential counts have been believed by some to be an aid, but the whole question still remains to be settled. A rise in the blood pressure has been thought by Crile[41] to be an indication of perforation, and from a study of 5 cases he concludes that there is a rise in the pressure after perforation to the same high level as occurs in peritonitis from other causes—a view that is shared by Sheppard,[42] Rochester,[43] and others.

The symptoms of general peritonitis, the result of the perforation of a typhoid ulcer, are in no way different from those of a general peritonitis of different etiology. Their onset is usually to be observed in from four to six hours after the time of perforation, and presents a clinical picture so well known as to need no description here.

Diagnosis. The ideal would be to make the diagnosis in what Cushing[44] calls the "pre-perforative stage;" but this period in the fulminant cases may be so short as to pass unnoticed as a clinical entity. It may be further obscured by the fact, as Killiani[45] has shown, that the perforation may involve other viscera, such as the gall-bladder, simultaneously with the intestine. Then, too, perforation may be simulated by other conditions: Miller[46] notes 2 cases of fecal impaction in children which gave the symptoms of an intra-abdominal calamity; Hall,[47] a case in which perforation was simulated after the administration of a medicinal dose of opium; Scudder,[48] a series of cases of mistaken diagnoses.

The space at my disposal does not permit of the consideration in detail of the differential diagnosis of perforation from hemorrhage, cholecystitis, suppurating mesenteric gland, and iliac or femoral thrombosis. While every effort should be made to make a correct diagnosis, too much emphasis cannot be laid upon the fact that all important is the recognition of the fact that some intra-abdominal calamity has occurred that demands immediate operative interference for its relief. Occasionally cases of perforation may recover without an operation; Miller[49] has noted such a case in which the perfo-

[39] Trans. Assoc. of Amer. Phys., 1900, xv, 82.
[40] Johns Hopkins Hospital Reports, 1894–1895, p. 83.
[41] Jour. Amer. Med. Assoc., 1903, xl, 1292.
[42] Lancet, 1907, i, 1293.
[43] Personal communication.
[44] Annals of Surgery, 1901, xxxiii, 544.
[45] Ibid., 1907, xlv, 38.
[46] Archiv. of Pediat., 1906, xxiii, 441.
[47] Jour. Amer. Med. Assoc., December 8, 1906.
[48] Boston Med. and Surg. Jour., July 18, 1907.
[49] Ibid., May 25, 1899.

ration became sealed by an adherent tag of omentum; Brown,[50] another similar case; Musser,[51] a case in which a perforaton of the ileum was closed by adhesion to the posterior wall of the bladder. Price[52] states as his belief that the reports of recovery from perforation without operation are entirely too numerous to be true.

PROGNOSIS. The prognosis of necessity bears a distinct relation to the rapidity with which the diagnosis is made and operation performed, and to the bacteriology of the resulting peritonitis. As a general rule this is due to the colon bacillus, more rarely to the typhoid bacillus or to virulent organisms such as the streptococci. Vincent,[53] Flexner and Fraenkel,[54] Dalziel,[55] and others have all emphasized the fact that the streptococcic infections of the peritoneum are practically always fatal.

TREATMENT. An immediate operation should be the rule in all cases of perforation, unless the subject is dying. Occasionally patients have recovered that have been operated upon some time after the occurrence of the perforation: thus, Lauper[56] notes one on which he operated successfully fifty-eight hours after the perforation, and Moschowitz[57] another successful case, which came to operation three and one-half days after the apparent time of perforation.

As regards the anesthetic, there is a choice between local and general anesthesia. Local anesthesia has been used with success in some cases, but the use of ether would seem to be preferable, as it tends to diminish shock. It is all important that the operation should be speedily performed.

The more generally employed incision is that through the outer half of the right rectus muscle. As soon as the peritoneal cavity is opened a methodical search should be made for the perforation. The ileum should first be found and examined, as that is the most common location of the lesion.

The hole in the intestine may be treated either by suture, enterostomy, or resection. When closure can be accomplished without too great narrowing of the lumen of the bowel, Lembert sutures, preferably of silk, may be employed. It is a needless waste of time to excise the ulcer. In those cases in which the closure by suture is not practicable, enterostomy is indicated; the subsequent closure of the artificial anus is usually safely accomplished. This method was first proposed by Escher,[58] and has since been strongly advo-

[50] Annals of Surgery, March, 1903.
[51] Pennsylvania Medical Journal, April, 1905.
[52] American Journal of Obstetrics, 1907, lvi, 691.
[53] Anal. de l'Institut Pasteur, vii, 141.
[54] Johns Hopkins Hospital Reports, 1895.
[55] Glasgow Medical Journal, 1905, lxiv, 262.
[56] Corbl. f. Schw. Aertze, 1905, xxv, 74.
[57] New York Med. Monat., 1904, xvi, 402.
[58] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1903, xi, 4.

cated by Bartlett,[59] Hays,[60] and others. Anderson[61] states that the toxemia from a paralyzed bowel is a big factor in the mortality of perforation cases, and that this is an indication for a drainage rather than a suture operation, a view that has been concurred in by Domela.[62] The objection to the operation of resection is its great mortality. The peritoneal cavity should be flushed out with quantities of either hot salt solution or sterile water, and the operation completed by the introduction of drainage. Scott,[63] Blake,[64] and others, while insisting on the value of the Murphy method of enteroclysis, are opposed to the use of the Fowler position, as in their experience it has seemed to be productive of distinct harm. On the other hand, Hays,[65] who has had a large experience and very great success with his cases, states that he invariably employs it in an exaggerated form, the patient being placed almost upright in bed.

Conclusions. Too much stress cannot be laid upon the fact that all important is an early diagnosis and immediate operation. This would seem to be best attained by a close coöperation between physicians and surgeons, so that the latter, when the complication occurs, may not be at the disadvantage of not having seen the patient before. While typhoid fever in the past has been regarded as a disease belonging essentially to the realm of internal medicine, in the light of our further knowledge one may state that its relation to surgery is indeed most intimate. Holscher[66] studied the results of autopsies upon 2000 cases of typhoid fever and found that only 24 per cent. died from the fever per se, and the remaining 76 per cent. died as the result of the various sequels. Flexner[67] notes that in 80 per cent. of the cases of typhoid fever the bacillus can be shown in the blood of the patient during life; Busquet[68] has recently reported a series of 43 cases in which he noted it in the blood in pure culture.

That typhoid fever patients stand surgical interference well has been admirably illustrated by the case reported by Cushing, in which the patient was operated upon three times within two weeks: twice for perforation and once for intestinal obstruction from adhesions, and yet recovered. Scott[69] reports the case of a boy, aged eight years, who at operation presented two perforations of the ileum and a gangrenous and perforated appendix and still made a good recovery despite three relapses.

[59] International Journal of Surgery, 1904, xvii, 99.
[60] Personal communication.
[61] American Medicine, December 31, 1904.
[62] Rev. de gynec. et de chir. abdom., 1905, ix, 623.
[63] International Clinics, viii, 21.
[64] New York Medical Journal, February 23, 1907.
[65] Personal communication.
[66] Münch. med. Woch., 1891, xxxviii, 43.
[67] Journal of Pathology and Bacteriology, 1894, iii, 202.
[68] La presse méd., 1902, p. 593.
[69] University of Pennsylvania Medical Bulletin, May–June, 1905.

Summary of Statistics.

Number of operative cases	369
Died	242
Mortality percentage	65.58

Age.

Under thirty-one years	249
Over thirty-one years	75
Not stated	45
Total	369

Youngest patient aged five years; oldest, aged sixty-five years.

	Cured.	Died.	Mortality percentage.
Children	37	31	45.58
Adults	75	178	70.03
Not stated	15	33	68.77
Total	127	242	65.58

Sex.

Males	281
Females	58
Not stated	30
Total	369

Location of the Perforation.

Stomach	1
Jejunum	1
Meckel's diverticulum	2
Ileum	279
Cecum	5
Appendix	15
Colon	12
Not stated	54
Total	369

Perforation of the Appendix.

Sex.

Males	9
Females	5
Not stated	1
Total	15

Results of Operation; Perforation of the Appendix.

	Cured.	Died.	Mortality percentage.
Adults	6	3	33.33
Children	4	0	..
Not stated	0	2	100.00
Total	10	5	33.33

Number of cases with multiple perforations	31
Greatest number in a single case	5

Treatment of Perforation.

	Cured.	Died.	Mortality percentage.
Suture	108	223	70.38
Enterostomy	9	11	55.00
Resection	0	3	100.00
Appendectomy	10	5	33.33
Total	127	242	65.58

Cases of Inflammation of the Appendix Submitted to Operation.

	Cured.	Died.	Mortality percentage.
Adults	10	3	23.07
Children	4	1	20.00
Not stated	4	0	00.00
Total	18	4	18.18

SPASM OF THE CHEST MUSCLES, PARTICULARLY THE INTERCOSTALS, AS A PHYSICAL SIGN OF DISEASE OF THE LUNGS.

By F. M. Pottenger, A.M., M.D.,
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Muscle rigidity has long been considered an important symptom in certain diseases, especially acute disease of the abdominal organs. This muscular spasm or rigidity varies in location according to the organ diseased: thus, if the appendix is inflamed, the rigidity is found in the right lower quadrant of the abdomen; if the gall bladder, in the right rectus; if gastric perforation or pancreatic disease be present, in the upper portion of the left rectus; and when general peritonitis is present, the abdominal muscles generally show rigidity. Spasm of the lumbar muscles is noticed in pyelonephritis, and spasm of muscles about the joints is an important symptom accompanying tuberculosis of the joints. So far, I have not been able to find mention of rigidity of the chest muscles as a sign of inflammation of the lungs. Musser[1] mentions the fact that spasm of the thoracic muscles occurs over the affected side in pleuritis, but does not mention its occurrrence when the parenchyma of the lung is involved. Mackenzie[2] explains the sense of constriction experienced during attacks of angina pectoris as being due to spasm of the intercostal muscles through reflex stimulation.

In the examination of patients suffering from pulmonary tuberculosis, I have found this muscle rigidity, particularly as it affects the intercostal muscles, to be a constant sign. Not only have I been able to map out the areas of infection, but I have been able

[1] Medical Diagnosis.

[2] Diseases of the Heart.

to judge the nature of infiltration with a considerable degree of accuracy by the condition of the muscles, the rigidity being much greater over dense infiltrations than over infiltrations of less degree, and greater over recent inflammatory infiltrations than over old quiescent ones.

There is some question in my mind as to the exact explanation of these rigidities. It is easy enough to say that they are due to nerve irritation, but to trace accurately the paths through which the stimuli are conveyed is somewhat difficult; and the fact that the rigidity is so often confined to the muscles or even parts of muscles which immediately overlie the inflamed parts, seems to me to be unsatisfactorily explained by their nearness, and not explained at all by saying it is due to direct stimulation of the nerve trunks supplying the part, for other muscles or other parts of muscles supplied by the same nerve trunk as the muscle or portion of muscle which shows the rigidity, show none at all. A very good illustration of this is found in the rigidity in the upper portion of the left rectus in the presence of gastric perforation or acute pancreatitis. While the entire rectus is supplied by the lower intercostal nerves, the rigidity for the most part is confined to the upper portion of the muscle. It has been suggested that the areas showing greatest rigidity represent the fields of maximum response, but this fails to convey a clear, definite idea to the mind.

Neither can this be explained by the supposed and oft-repeated explanation of the rigidity of the abdominal muscles in the presence of acute inflammations of the abdominal organs: that it is Nature's method of protecting an inflamed part. This does not explain. It is simply a confession of ignorance in the guise of an explanation. It might be said with equal justice of the stiffness of an inflamed joint, and often is, that it is an illustration of the beneficence of Nature—that Nature has put the joint to rest in order to protect it; when the truth of the matter is that the stiffness is due to the products of inflammation being thrown out around and into the joint, and that it is an unavoidable condition without any respect whatever for the patient's welfare. In diseases of the chest such a supposed explanation falls of its own account; for what extra protection could the intercostals and other chest muscles give to the inflamed organs in the thorax over and above that furnished by the bony cage in which they are placed? It seems more probable that there is some direct nerve connection, perhaps of developmental origin, between the underlying organs and the special branch of the nerve which supplies the muscles overlying them, whereby impulses may travel without stimulating other muscles supplied by the same general nerve trunk. If this be true, we can see that while all the abdominal muscles are supplied by the lower intercostal nerves, and all the abdominal viscera are supplied by the sympathetic system, yet an appendicitis can stimulate the muscles in the lower right

quadrant of the abdomen, and pancreatitis the upper half of the left rectus, without stimulating the abdominal muscles in general, and an inflamed area in the lung or pleura might cause a spasm of the overlying muscles without stimulating all the muscles supplied by the same nerve trunk.

It may be argued that the rigidity of the intercostal muscles that I have in mind is the same as has been described heretofore as due to pleuritis; but there are certain facts which speak against this. There is a rigidity that can be noticed over pleuritis, but it differs in degree from that noted when there is inflammation of the parenchyma of the lung. In the latter instance there is a much greater resistance, the degree agreeing very accurately with the percussion findings. The analogy of the abdominal conditions, which are accompanied by muscle rigidity, also speaks against the involvement of the underlying pleura as a necessary cause of the rigidity. In appendicitis the rigidity of the abdominal muscles is present when the inflammation is confined to the organ itself and the parietal peritoneum is free from disease. The same is true in gall-bladder disease and pancreatitis; so that it seems that inflammation of a contiguous part is not necessary to produce these muscular spasms.

The intercostal rigidity must not be confused with the feeling of resistance found over non-air-containing organs like the liver and heart. These organs can be outlined with more or less accuracy by palpating the intercostal spaces, but the sense conveyed to the touch over the heart or liver is very different from that experienced on palpating the rigid intercostals over pulmonary infiltrations.

That this is a true muscle spasm, and not dependent upon the thickness of the muscles themselves, can be easily determined by careful observation: if when examining a patient with pulmonary tuberculosis the examiner will carefully palpate the intercostal spaces, he will notice different degrees of rigidity over different areas of lung tissue; but allowing for the different thickness of the muscles and overlying tissues, it is still evident that the difference noticed by the touch is due to the condition of the muscles themselves and not to the thickness of the tissues.

While rigidity affects all the muscles of the chest, yet it is found in greatest degree in the intercostals. Rigidity in the superficial muscles may be detected by picking them up and rolling them between the thumb and fingers, when it shows as an increased firmness. In some instances the rigidity is so marked that it can be easily detected by the sense of firmness to the touch as compared with the softness of the muscles over healthy tissues. While the rigidity of the superficial muscles is at times very marked, yet I have found that of the intercostals of greatest value in diagnosis, except at the apices where the mass of muscles covering the superior aperture of the thorax may be relied upon.

In some instances not only are the motor nerves affected, but the sensory nerves also, in which cases the overlying skin is hypersensitive. Patients so affected often complain of pain when the skin is touched, and they are especially sensitive to the percussion strokes. This is often considered a nervous manifestation and ignored, but we have every reason to believe that it is painful.

What has seemed to me to be the best method of detecting the intercostal rigidity is a systematic palpation of the intercostal spaces, beginning at the lowest and comparing the rigidity of each space with the one above and also with the corresponding space on the other side. A little practice will soon show the examiner that he must allow something for the natural increased resistance over the heart and liver and also over thick muscles, such as the pectorals. The palpation is best done by gently pressing the tips of the fingers into the intercostal spaces and moving the hand sidewise while noting the degree of resistance. During this procedure the fingers should not be allowed to slip on the skin, for it is the condition of the muscle and not of the skin that is to be noted.

In examining many advanced cases of pulmonary tuberculosis, I have found that when the tissues break down and form a superficial cavity the resistance which was formerly noted disappears. I cannot believe that this indicates that the muscle rigidity has disappeared, for I believe this is more or less permanent. The explanation which seems to me probable is that the disappearance of resistance is due to the removal of the densely infiltrated tissues which have previously furnished support for the intercostals. That it is not due to a disappearance of the muscular spasm is supported by the fact that the rigidity does not disappear (at least not always) in old lesions, as, for example, in the instance mentioned later, in which the rigidity was found twenty-four years after the history of acute symptoms.

Not only does this spasm of the chest muscles bid fair to be an important physical sign in itself, but it helps to explain other well-recognized signs: lagging on the affected side, contraction of the chest wall, ankylosis of the costosternal articulation, diminution of the respiratory murmur, and the harsh, impaired respiratory note. It is obvious that spasm of the chest muscles must interfere with the free movement of the ribs, thus limiting the motion on the affected side and interfering with the normal expansion of the lung. We have been of the opinion that lagging is due to an interference with the normal elasticity of the lung tissue, owing to the presence of tubercles; but it seems that this muscular spasm adds another important and perhaps even greater factor. The connection between lagging and muscular spasm raises the question of the earliness in the disease in which this sign appears. Lagging is one of the most constant as well as one of the earliest signs noted in pulmonary tuberculosis. It is found before the presence of rales, when the

only changes found upon auscultation are so slight that they can be detected only by the most careful examination; and it remains throughout the disease. So far I have been able to detect muscle rigidity above the clavicle and spine of the scapula, or in the first intercostal space in every early case that I have examined. While the number is too small to warrant a general conclusion, yet this indicates that the sign comes very early in the disease, and, of course, this is what we should expect. It is much more difficult to detect in these slight infections, and requires more skill and more care on the part of the examiner. How long it persists after activity ceases remains to be determined. Recently I had an opportunity to examine a man who had not had any active symptoms in the lung, as far as could be determined from his history, for twenty-four years, but I was able to outline his former trouble by the rigidity of the intercostals. Very marked lagging was present over the area which had been diseased. Percussion and auscultation proved the accuracy of the findings on palpation. While more observations are desirable before giving an opinion, this indicates that the sign is not an indication of active disease, but that it points to the fact that the underlying tissues are or have been diseased. While the intercostal muscles are not very large, and while their contractile power is not very great, yet it is evident that their constant contraction, reinforced by the less degree of contraction of the more superficial chest muscles, must have a tendency to lessen the thoracic space, thus causing the contraction or flattening which is so common in chronic pulmonary conditions. This same interference with motion of the ribs hinders expansion of the lungs and helps cause the auscultatory phenomena mentioned above.

The fact that this rigidity remains so long and is so constant needs explanation. It is contrary to the teachings of physiology that a muscle should remain in a constant state of contraction; sooner or later the contractile power is overcome, and relaxation ensues. That this does not occur in old lesions indicates that there is probably some pathological change, perhaps a fibrous degeneration which takes place in the muscles which preserves their rigidity.

A new physical sign is of no special importance beyond the scientific interest attached to it, unless it is a distinct aid to diagnosis. This, I believe, intercostal rigidity to be. Modern advances in diagnosis of diseases of the chest have had a tendency to belittle the value of physical examination. So many men had realized the difficulty of making accurate diagnoses by the usual physical examinations that when the microscope proved its value in diagnosticating tuberculosis they ceased making careful physical examinations and depended almost entirely on the microscopic findings. The tuberculin test as administered today hypodermically, by the skin and conjunctiva, will have a tendency further to discourage careful

physical examination. This is greatly to be deplored, for approximately accurate diagnoses of pulmonary conditions can be made only after careful physical examination.

I hope that this sign may be of value, but I would add one word of caution as to technique: that is, not to lay the fingers flat on the chest, but to palpate with the ends of the fingers gently pressed into the intercostal spaces. The examiner will often be confused when pleuritis exists, for, as mentioned above, pleuritis produces a rigidity, but this can be excluded by other methods. It will also be difficult to interpret at times in chests which have been the seat of many and varied changes, such as we find in far advanced tuberculosis. But in these instances it is not different from other methods of physical examination, for they all fail us under such conditions. A little experience will show one its worth and also its limitations.

GASTRIC DIGESTION IN INFANTS.

A REVIEW OF THE LITERATURE.

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The investigations into the chemical and physiological processes which go on in the stomach of the human infant during the progress of digestion, may be divided chronologically into two groups: investigations before and after the introduction of the stomach tube. The studies of the first period were few and of but little value; they consisted in investigations on the lower animals and upon the cadaver of the human infant. The objections to the first of these methods depend upon the facts that at birth the digestion of the lower animal is in a more advanced state of maturity than is the case in the human being, and develops much more rapidly to the adult type, so that one is not justified in drawing absolute conclusions from animal experiments. The study of the stomach and gastric contents of the dead baby are open to the fallacies that whatever causes the death may markedly alter the constitution of the gastric juice, the condition being rather pathological than physiological, and that the gastric mucous membrane degenerates so rapidly after life has ceased that the state at autopsy may be markedly different from that occurring during life. However, one or two observations were made during this period which are of some interest, the most important being the finding by Zweifel,[1] in 1874,

[1] Untersuchen über den Verdauungsapparat der Neugeboren, 1874.

of an acid in an extract of the gastric mucous membrane of a still-born child, the nature of which, however, he was unable to determine; and by Langendorff,[2] in 1879, of pepsin in a three months' fœtus. He could not, however, find acid in a fœtus of six months.

The studies of real value, however, have been made by the use of the stomach tube. This instrument, though first introduced into medicine by Kussmaul,[3] in 1867, for the study of the contents of the stomach of the adult, was not used for children until many years later, when Epstein,[4] in 1880 and again in 1883, published papers describing the ease with which a small rubber catheter could be passed into the stomach of even the youngest infant, and strongly recommended lavage as a therapeutic measure in the gastro-intestinal diseases of infancy. He, however, did not attempt any examination of the contents, and to Raudnitz,[5] in 1887, twenty years after Kussmaul's first use of the tube on the adult, belongs the credit of first having made a chemical examination of the gastric contents of an infant by the use of the stomach tube. This author, however, examined but seven cases, and these for the rennin action only, so that the credit of the first systematic chemical investigation belongs to Leo,[6] who in 1888 published his report of the study of 134 cases. The following year von Puteran,[7] in St. Petersburg, reported 1027 examinations on 248 healthy children under six weeks of age. These papers aroused much interest, and during the next two years seven papers appeared, covering various aspects of the subject. Since then each year or so some new publication has appeared adding more or less to our knowledge. The subject may be considered under four headings: motility, acidity, pepsin digestion, and rennin coagulation.

Motility. The subject of the motility of the infant stomach has been studied by two methods, the length of time that it takes the organ to empty itself, and the number of minutes after a meal before food appears in the intestines. In Epstein's original article, though he made no chemical examination of the stomach contents, he did note the average time which food remained in the stomach, and stated that in healthy breast-fed children, food could be found from an hour to an hour and a half after a meal, while in children suffering from gastro-enteritis it remained from two to five hours. Leo in 1888 elicited the following facts: With breast-fed children of less than a week old, the stomach is often empty in one hour, while during the first month the maximum duration of the food in the stomach is one and one half hours. With older children, and children fed on cows' milk, it remains from one and a half to two hours. He agreed with Epstein that in disease the time is much longer, and in one case he found a considerable quantity after seven

[2] Archiv f. Anat. und Physiologie, 1879.
[3] Prag. med. Woch., 1880.
[4] Arch. f. Kindh., vol. iv.
[5] Prag. med. Woch., 1887, No. 24.
[6] Berl. klin. Woch., 1880, xxv, 980.
[7] Thesis, St. Petersburg, 1889.

and a quarter hours. Leo further showed that the stomach is never entirely empty, but that some time after the last traces of food have disappeared a few drops of a thick yellowish fluid could be obtained by the stomach tube. This fluid contained all the elements of gastric juice in a very concentrated form. To prove whether this was due to further secretion, or was the remains of the last meal, Leo washed several stomachs quite clean, and then passed the tube again a half-hour later. The fluid then obtained was neutral, and consisted apparently merely of a little of the wash water. From this he inferred that no secretion occurred in the empty stomach, and that the fluid formed therein was gastric juice remaining from the last meal, concentrated by the absorption of the water.

Von Puteran, in 1889, in his 248 breast-fed children under six weeks of age found the stomach practically empty in seventy minutes in 3 per cent. of his cases, in ninety minutes in 30 per cent., and in two hours in 95 per cent. He could, however, find traces of food as late as two and one-half hours after the last meal.

Einhorn,[8] in 1889, studied the effect of various foods upon digestion, his method being to wash the stomach on alternate days, one day in one and one-half hours and the other in two hours. On a diet of breast milk he found the stomach always empty in two hours. He was unable to repeat this at an earlier hour, as the mothers objected to the procedure. On a diet of cows' milk and water, and cows' milk and barley water, the stomach emptied itself in from one and a quarter to two hours, while on various artificial foods, including Carnack's, Nestle's, and Mellin's foods, and malted milk, considerable quantities remained after two hours.

Cassel,[9] in 1890, confirmed the finding of Epstein and Leo in regard to the long duration of food in illnesses. He studied seven children from four weeks to eight months of age suffering from marasmus, and found that it took from four to six hours to complete the gastric digestion.

Czerny[10] added one more fact to our knowledge in 1893, by showing that while a child fed on breast milk every four hours emptied his stomach in from one to one and a half hours, if two or three feedings were given at intervals of an hour, food could be found in the stomach after the last feeding for a much longer period. From this he inferred that the stomach, like the other organs of the body, required periods of rest properly to fulfil its function.

Pfannersill,[11] in 1893, made the first observation on the time required for food to appear in the intestines. For this purpose he used the common salol test, giving the child salol mixed with its

[8] New York Med. Jour., 1889, p. 67.
[9] Arch. f. Kindh., 1890, xii, 175.
[10] Prag. med. Woch., 1893, p. 495.
[11] Jahrb. f. Kindh., xxxv, 369.

food. He passed a catheter on the infant and left it in situ, testing the urine every five minutes with ferric chloride. By this procedure he obtained the iron reaction in from forty to sixty minutes in sixty healthy and twenty-seven ill children. In the healthy children the reaction continued for from twenty-four to twenty-six hours, while with the ill children it lasted much longer, even up to one hundred and forty-four hours in one case.

Hecker,[12] in 1900, by the same method found that the appearance of the reaction in the urine varied with the age of the patient. In children from one to three years old it averaged forty-five minutes; from three to five, fifty-eight minutes; from six to ten, seventy-three minutes.

Acidity. The first study of the acidity of the infant's stomach contents was made by Leo, in 1888, who investigated thirty healthy children on various diets, between two hours and twelve months of age, and one hundred and four children suffering from gastro-intestinal diseases. He found that the reaction of the stomach contents to litmus immediately after a meal was the same as that of the ingested food, that in fifteen minutes it was weakly acid, and that the acidity increased steadily during the period of digestion. He was unable, however, to detect the presence of free hydrochloric acid until an hour or more had elapsed; on the other hand the empty stomach always contained the free acid. In two newborn children, before any food had been taken, a small amount of brown bloody fluid was obtained which was strongly acid and contained free HCl, whereas the reaction of the amniotic fluid is alkaline. In his cases suffering from gastro-intestinal diseases, the contents also were acid, and often highly so, containing besides the hydrochloric, butyric, acetic, and lactic acids. This high acidity, and especially the presence of the large amounts of hydrochloric acid, Leo laid not to a hypersecretion, but to the long continuance of the food in the stomach. He then described for the first time what he called the "binding power" of milk for hydrochloric acid. He showed that considerable amounts of hydrochloric acid must be added to a neutral or amphoteric milk before any reaction for the free acid could be obtained. By this he explained the fact that the acid does not appear in a free state until so late in digestion, so that it would not show itself until after the milk had become saturated with it.

Van Puteran in his investigations on breast-fed babies under six weeks of age confirmed the steady increase of total acidity during digestion varying from 0.3 per cent. in ten minutes to 0.8 per cent. in ninety minutes. In his cases he never found fatty acids, and lactic acid only once.

Einhorn showed that the total acidity was variable, but in general

[12] Jahrb. f. Kindn., lvi, 657.

lower in children fed on mothers' milk than in those on cows' milk or artificial foods. He found lactic acid in most of his cases, and free hydrochloric acid only once in fifty examinations.

Von Jaksch,[13] in 1890, published a paper in which he differed from the previous authors in finding free hydrochloric acid in fifteen minutes to the amount of 0.08 per cent., in thirty minutes 2.4 per cent., and in one hour 2.9 per cent. His method was to take 10 c.c. of the stomach contents and to this add an excess of $BaCO_3$. This he evaporated on the water bath in a p.atinum dish, dried and heated to a red glow over the free flame. The residue was then taken up in water, boiled and filtered. The $BaCl_2$ so formed went into solution, while the $BaCO_3$, formed from the organic acids, remained on the filter. The barium in the filtrate was then estimated as $BaSO_4$ and the amount of chlorides calculated. It is evident that by this method von Jaksch obtained not only the free hydrochloric acid, but also the acid which was bound to the casein, and his figures represent the free plus the bound HCl.

Cassel in his marasmus cases found free HCl in about half of the patients, and confirmed Leo's finding of butyric acid.

Pipping[14] writing from Finland, in 1891, reported investigations on twenty-nine healthy children under three months, and twenty-five others suffering from gastro-intestinal troubles, and gives the following findings: In healthy breast-fed children, he in no case found either lactic or butyric acid. In healthy children fed on cows' milk, lactic acid occurred in about one-half of the cases and the fatty acids in all. In the ill children on mothers' milk, lactic acid was present in three-fourths of the cases and fatty acids in one-fourth, while in ill children on cows' milk, lactic acid occurred in none, but the fatty acids in two cases in which examinations were made.

Heubner,[15] in 1891, examined forty babies of various ages and on various diets, with especial reference to the forms of acids found in the stomach. His method was to wash the stomach clean with distilled water. This wash water was then distilled, and the distillate titrated for the volatile fatty acids. The residue was shaken with ether and the ether titrated for lactic acid. He tested for the free hydrochloric acid by using phloroglucin-vanillin, and Congo red as indicators. By this method he found volatile acids in about one-half of the twenty-six cases in which they were looked for, and in measurable quantities in five of them. Lactic acid could be demonstrated in all cases which were on a milk diet. As to free hydrochloric acid, in the twenty-six cases in which enough material was obtained for a quantitative estimation, it was found in measur-

[13] Ztschr. f. klin. Med., xvii, 382.
[14] Thesis, Helsingfors, 1891.
[15] Jahrb. f. Kindh., 1891, xxxii, 27

able amounts in two cases, and in traces in four others. In the cases in which the meal had remained longer in the stomach, in which the small amount of material allowed qualitative examination only, it was positive for free HCl in one-half of the cases. Heubner then took up Leo's binding power of milk and found that 100 c.c. of cows' milk would absorb 0.324 gram of HCl before a reaction for this free acid appeared, whereas woman's milk would absorb only about half that amount.

In the same year Wohlman[16] in a series of experiments came to the conclusion that if the stomach was washed out previous to the giving of the food, and then examined in one and a half hours, the amount of HCl was increased on an average of 85 per cent. over that found when no previous lavage had been done. This he thought was due to the irritation of the mucous membrane stimulating an increased secretion. He further found that in indigestion the HCl increased in amount during digestion, but at a slower rate than in health. In prematurely born children he could find no free HCl at any time. A tea diet gave the presence of free HCl at an earlier hour than a milk diet.

Clopatt,[17] 1892, and Henri and Marcel Labbé,[18] 1897, first made use of the method of Hayem and Winter to estimate not only the total acidity and the free HCl, but also the total chlorides, fixed chlorides, and organically bound chlorides. Their results were not very striking, Clopatt saying that he could find no relation between the acidity and the age of the child or the time the food remained in the stomach. The Labbés, on the other hand, found the total acidity to be very feeble at birth, to increase rapidly during the first month of life, and then more slowly afterward.

In 1898 Bauer and Deutch,[19] in Budapest, studied the occurrence of free HCl in various diseases. Their most interesting findings relate to pneumonia and diphtheria. They found that if the stomach contents was removed in from one and a half to two hours after a meal during the febrile period of pneumonia, no free acid could be found, whereas immediately after the crisis it reappeared. In diphtheria, during the attack, the free acid disappeared, and in cases which recovered without the use of antitoxin, did not reappear until about the third week. In cases also in which serum was used, but the patient died, the free acid never returned, while in these cases in which the use of antitoxin was to be followed by recovery, the acid returned to the stomach in from twenty-four to forty-eight hours after the injection.

Meyer,[20] Copenhagen, in 1903, published an extensive piece of work, in which he recommended the use of a constant test meal in studying infant digestion, and advised the use of barley water as

[16] Jahrb. f. Kindh., 1891, xxxii, 297.
[17] Revue de méd., 1892, p. 249.
[18] Revue mens. des malades des enfants, 1897, p. 401.
[19] Jahrb. f. Kindh., 1898, xlviii, 22.
[20] Arch. f. Kindh., xxxv, 79.

being of especial value, as by its use neither lactic nor butyric acid is formed, so the HCl secretion can better be studied. He differed with Wohlman's statement that lavage previous to the giving of the meal increases the amount of acid secretion. In his series of cases, in which lavage was performed a half hour before the meal, no such increase occurred. Meyer found that while there was a general progressive increase in acidity during digestion, very marked variations occurred from day to day in the same child on the same diet, due, he thinks, to a neurotic influence. The highest total acidity which he could find on barley water diet was 0.9 per cent., on distilled water 0.8 per cent., while on cows' milk it went much higher, even to 2.58 per cent. in one case. In cases of acute and chronic gastritis on the barley water diet he found the acidity to be below normal, while neither lactic nor butyric acid could be found.

The paper of Hamberger and Sperck,[21] which appeared from Escherich's clinic in Vienna, in 1905, is of interest, as all their subjects were under two weeks of age, and were fed on mothers' milk. They agreed with the increase in amount of free HCl during digestion, finding it present at the end of one hour in 10 per cent. of the cases, in one and a quarter hours in 33 per cent., and in two and a half hours in 50 per cent. In these very young infants they never found lactic or butyric acid present. They lay much stress upon what they call the hydrochloric acid deficiency of the stomach contents.

Following Sjöquist's findings, that it is the hydrochloric acid only which is bound to the protein that acts in peptic digestion, and that the appearance of free HCl signifies that enough has appeared to carry on the digestive process to its completion, they argue that it is of importance to know how far the contents are below the point of complete saturation with the acid. To decide this they added decinormal acid until it showed free in the contents. The amount required they called "hydrochloric acid deficiency of the contents." They then said that the "hydrochloric acid binding power" of the material was equal to the total acidity plus the hydrochloric acid deficiency, or if free acid is present, the total acidity minus the free acid. They then stated that a priori one would expect the binding power of the contents to be less than that of the food ingested, due to its dilution by the gastric juice. This, however, does not occur, 100 c.c. of breast milk having a binding power for 60 c.c. $\frac{n}{10}$ HCl, while the stomach contents has a binding power of 80 c.c. To explain this they offer two hypotheses: one, that the hydrolytic splitting of the protein enables the larger number of molecules to take up more acid (this they discard, as they say it does not occur in artificial digestion), and the other, that the increased binding power is due to a greater concentration of

[21] Jahrb. f. Kindh., 1905, lxii, 495.

the stomach contents by the absorption of water. If it is due to the withdrawal of water alone, one would expect a concentration of the insoluble elements of the stomach contents, that is, the coagulated albumin, and as most of the fat is imprisoned in the coagulum, an increase in the concentration of fat. Then too the sugar should be in a stronger solution. The percentage of sugar, however, is found to be decreased, and that of the fat is unchanged. They therefore, infer that the increased HCl binding power is due neither to protein splitting nor to concentration of the contents, but to the secretion of acid salts and weak organic acids, and possibility to the formation of fatty acids by a fat-splitting enzyme in the stomach.

Sedgewick,[22] of Minneapolis, working in Heubner's clinic in Berlin, in 1906, made a study of the occurrence of a fat-splitting enzyme in the stomach contents of infants and newborn rabbits, from which he drew the following conclusions: (1) A fat-splitting enzyme occurs in the stomach of the infant; (2) it appears early in the first twenty-four hours in the rabbit, and as early as the second week in the infant; (3) it can reach as high a grade as in the adult; and (4) this can explain a part of the acidity of the stomach contents.

Miller and Willcox,[23] in London, published some results in 1907, according to which they divide "wasted infants" into three classes: (1) Simple marasmus or atrophic dyspepsia, with a reduction in the acidity and pepsin content; (2) hypertrophic stenosis, in which the acid content is also low; and (3) acid dyspepsia or pylorospasm, in which the acid content is high.

The most recent addition to the knowledge of the gastric contents of the infant comes from the clinic of Prof. Schlossmann, in a work by Engel.[24] This author investigated the gastric secretion in an infant, aged five weeks, who was suffering from pylorospasm, upon whom a jejunal fistula had been made, through which the child was fed. By passing the stomach tube he obtained pure gastric juice. He estimated that from 100 to 200 c.c. of gastric juice was secreted daily, and that it differed very slightly in acid and pepsin content from the gastric contents of the adult. The figure which he gives for the free hydrochloric acid (0.257 per cent.), while not differing markedly from the normal in the adult, constitutes a very marked hyperchlorhydria for an infant of this age. This agrees with the cases of Knobfelmacher,[25] in which pylorospasm was accompanied by marked hyperchlorhydria.

Protein Digestion. Escherich, in the early days of the study of the digestive action of the stomach of the infant, made the statement that the organ was practically inactive as a digestive organ, and acted merely as a reservoir, or holder of food, while the entire digestion of milk occurred in the intestines. Most of the investiga-

[22] Jahrb. f. Kindh., 1906, lxiv, 194.
[23] Lancet, 1907, ii, 1670.
[24] Archiv f. Kindh., 1908, xlix, p. 16.
[25] Wien. klin. Woch., 1900, p. 1188.

tions on protein digestion have been undertaken to disprove this statement. Leo was the first to prove that a protein splitting enzyme was present in the infant stomach, though he found that usually more acid had to be added, in order to enable the digestion to go on to any extent. He made two series of experiments. In the first he divided the material into two parts, one saturated immediately with ammonium sulphate; the other after twenty-four hours in the thermostat. He found very little difference between the amount of precipitate in the two cases, showing that for the amount of acid in the child's stomach, the peptic digestion was nearly complete at the time the meal was taken out. Addition of more acid enabled the proteolysis to go farther. He then investigated the stomach contents at different times during digestion. The specimen was first saturated with sodium chloride to remove what at that time was known as the primary propeptone. The filtrate from this was acidified to throw down the secondary propeptone, and the filtrate from this with phosphotungstic acid to get the peptone. Leo found by this method that a half hour after a meal there was an increase in the amount of albumoses, while peptones were present in traces only, whereas in an hour there appeared a marked increase of the secondary propeptone and peptones.

Van Puteran by a similar method showed that in his young breast-fed infants native albumin could rarely be found one hour after a meal, while peptone appeared in fifteen minutes. Cassel found that, if acidified, the stomach contents of his marasmus cases would always digest a flake of blood fibrin, even in the worst cases.

Toch,[26] in 1893, made an extensive study on two healthy and five ill children, and found peptone in all the cases. He then discussed the source of the peptone and said it must be produced from the casein by one of three actions: peptic digestion, hydrolysis by rennin, or the action of bacteria.

To determine which of these was the active agent, he performed the following experiments. He placed a piece of blood fibrin in a few cubic centimeters of freshly removed stomach contents and allowed it to stand in a thermostat for some hours. The fibrin remained unchanged; another piece placed in the same amount of contents, which had previously been acidified, was digested in a few hours. He therefore said that though pepsin was present in the stomach, it did not act in the absence of free acids, and as none of his cases showed the presence of the free acid, the peptone found in their stomachs could not have been produced by the action of the pepsin. To determine that the digestion was not due to bacteria, he shook some contents with chloroform water, which he proved made it sterile, and to this added fibrin. The results were the same: without acid, no action; with acid, complete digestion. By this

[26] Arch. f. Kindh., 1894, xvi.

means he threw out the bacterial action. His third experiment consisted of placing specimens of cows' milk and mothers' milk in test tubes and adding rennin to them. After some hours at body temperature peptones were found in all the specimens. Toch, therefore, concluded that the peptone in the stomach of the infant could not be the result of peptic digestion or bacterial action, but must have been formed by the rennin. He had apparently completely overlooked the communication of Pipping two years before, which showed that free hydrochloric acid was not necessary for peptic digestion, that bound to the protein acting quite as well. In the light of the finding his elaborate reasoning becomes thoroughly worthless.

A recent and accurate effort at a quantitative estimation of protein digestion in the infant stomach is that of Leo Langstein,[27] assistant to Professor Heubner, who, in 1905, made a study of the gastric contents of several healthy children. His method was to wash the stomach clean with a liter or so of distilled water. One part of this wash water he acidified and boiled to remove the albumin. A second part he saturated with zinc sulphate to remove the albumin and all fractions except the peptones. In aliquot parts of the filtrates from these two precipitates he estimated the nitrogen by the Kjeldahl method. He found that in his cases the nitrogen in the form of proteoses varied from 0.012 to 0.040, while that as peptone and residual nitrogen from 0.003 to 0.017. He tested all his specimens for the amino acids, but was never able to find them present. Langstein then referred to the work of Rotundi, in 1903, which proved that the protein fractions produced by the action of rennin on milk were those of the more complex structure only, and stood somewhere between native proteins and primary proteoses, and that by the enzyme peptones were never formed. Langstein took these facts as conclusive proof that the peptones formed in the infant's stomach were produced by pepsin digestion.

The first use of the new methods of pepsin estimation upon the gastric secretion of the infant was made by Rosenstern[28] in 1908, who used the ricin method proposed by Jacobi. He reached the following conclusions: The quantity of pepsin in the healthy artificially fed infant increases during the first four months of life, and then remains constant; healthy breast-fed infants appear to produce less pepsin than artificially fed infants of the same age; in children who are under weight the quantity of pepsin is in accord with the age, not the weight; diseases of digestion do not influence the pepsin secretion noticeably.

Reeves Ramsay,[29] working in Heubner's clinic, has recently pub-

[27] Jahrb. f. Kindh., 1906, lxiv, 139.
[28] Berl. klin. Woch., 1908, xlv, p. 542
[29] Jahrb. f. Kindh., 1908, p. 191.

lished the results of a study from which he concludes: (1) Pepsin is always present in the stomach of normal breast-fed infants; (2) pepsin is usually present in the stomach of nurslings suffering from acute digestive disorders; (3) pepsin and HCl are present in increased quantities in cases of pylorospasm; (4) pepsin is frequently absent in cases suffering from chronic atrophy; (5) pepsin reappears when these cases begin to improve; (6) the gastric juice of a normal child can convert protein into peptone without the addition of acid; (7) pepsin in the gastric juice is active in promoting digestion without the presence of HCl or lactic acid; and (8) HCl and lactic acid may be present in the stomach, with an absence of pepsin, and vice versa.

Rennin Coagulation. The investigations on rennin coagulation were inaugurated by Raudnitz in 1887, in his original work on the chemical examination of the stomach contents in the infant. He reports seven cases only, four between the age of one and seven days, and three from two to six months. He neutralized the entire gastric contents with sodium hydroxide, and to it added 50 c.c. of cows' milk. In his cases, in the first week of life, he obtained no coagulation, while in the older cases he always found it. Leo differed from him, finding rennin activity in the newborn as well as older children. Von Puteran in his long series of cases under six weeks, by adding 25 c.c. of cows' milk to 5 c.c. of the contents and keeping it at 40° C. for half an hour, could get no rennin coagulation in children under twenty-four days of age, while he always found the enzyme active after the thirtieth day of life. Sydelowski,[30] in 1892, agreed with Leo's findings that rennin could be demonstrated in the newborn and at all ages. He further found that the empty stomach contained it, as did the stomach in cases of marked marasmus, and finally Hamberger and Sperck report it present in all of their cases in the first week of life.

Resume. From these various investigations it will be seen that many and contradictory results have been obtained; a few facts, however, seem to be pretty definitely proved. In the first place, it may be said that all the factors present in the adult are found in a weaker form in the young infant. In the newborn child on breast milk the stomach usually empties itself in from an hour to an hour and a half; as the child grows older this time becomes longer. The few drops of gastric juice found in the empty stomach are the remains of that secreted during the last meal, and are not due to a secretion into the empty stomach. The motility is more rapid in breast-fed children than in those on cows' milk or artificial food, and more rapid in the healthy than in the ill child.

[30] Jahrb. f. Kindh., xxxiv, 612. Other articles not referred to in the text are: Wolff and Freedjung, Arch. für Kindrh., xxv, 161; Thiercelin, Paris, Thèse, 1894; Morcorvo, Paris, Thèse, 1889; and Francois, Paris, Thèse, 1907.

The acidity immediately after a meal is nil, but steadily increases during digestion, and is less in the very young than in the older. On a barley water diet free hydrochloric acid appears in the stomach in a few minutes, but on a milk diet it does not show itself for an hour or more, due to the fact that the casein absorbs it or combines with it in some way, and the free acid does not appear until the casein has taken up all required for its complete digestion. The free acid appears later in disease than in health, due to the increased amount of food in the stomach and to the slower secretion of the acid; in cases of pylorospasm the acidity is increased. Opinions differ as to the occurrence of lactic and volatile fatty acids, but these probably do not occur in healthy breast-fed infants, while in those ill or on cows' milk they are fairly common. Part of the acidity is probably due to a fat-splitting enzyme in the infant's stomach.

Pepsin is present at all ages and in all kinds of health, and acts in the infant stomach though to a less degree than in the adult. The peptic digestion goes on to the stage of peptones, but not beyond that. The fact that the stomach contents will not digest fibrin in the thermostat is due to the fact that all the hydrochloric acid is combined with the casein, and while the protein with which it is combined will be acted upon by the pepsin, a foreign protein without the addition of more acid will resist the enzyme.

Rennin occurs in the stomach after the first few weeks of life; whether during the first week is a moot question.

SYPHILIS OF THE STOMACH AND INTESTINES.

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Syphilis of the stomach, next to tuberculosis, the rarest of stomach diseases, was first described by Andral[1] in 1834. Since then, however, a number of cases have been reported, but the number of authenticated cases is still very small. Chiari,[2] for example, in 243 autopsies on syphilitic subjects, found only 2 undoubted cases of stomach syphilis. Stolper[3] and Fraenkel[4] report similarly to Chiari, but Aristoff,[5] on the other hand, maintains that careful histological

[1] Clinique médicale, Paris, 1834, ii, 201.
[2] Internat. Beit. z. Wiss. Med., Festschrift für R. Virchow, Berlin, 1891, vol. ii.
[3] Bibliotheca medica, 1896, Heft 6.
[4] Virchow's Archiv, Band clv.
[5] Ztsch. f. Heilkunde, Berlin, 1898, Band xix.

examination of the stomachs of luetic subjects frequently reveals syphilitic changes in the form of miliary gummas and diffuse syphilitic inflammation.

For many years all healed scars in the apices of the lungs were considered tuberculous; latterly, it has been recognized that many such scars are luetic in origin, that pulmonary syphilis is by no means so rare as it was formerly supposed to be. Similarly, more careful examinations will reveal the fact, as Aristoff has indicated, that gastric syphilis is not merely a medical curiosity. At present we may suspect specific stomach disease in all luetic subjects who have an intractable dyspepsia which does not yield to the ordinary procedures; but further than that we cannot go. There are no special symptoms which point to stomach syphilis except a definite luetic history and improvement under specific treatment—and even this last may prove deceptive, because we know that mercury and the iodides are alone sufficient to cause intractable dyspepsias, and that when they are discontinued the gastric symptoms abate. The only definite clinical symptom which may prove of value is the fact that the mucous membrane of syphilitic subjects bleeds very readily, and that the introduction of the stomach tube for diagnostic purposes is often followed by profuse hemorrhage. This is a secondary manifestation due to syphilitic hemorrhagic diathesis, and has been noted by Zeissel.[6] If in such cases an ordinary ulcer can be excluded, we may hit upon the real cause of the stomach trouble. This bleeding occurred in one of my own cases, and led to the suspicion of syphilis. Antiluetic treatment soon caused the patient's stubborn stomach disorder to disappear, and readily confirmed my suspicions as to the nature of the disease.

Gastric lues appears in three forms: (*a*) As syphilitic ulcer; (*b*) as syphilitic tumor; and (*c*) as syphilitic stenosis of the pylorus. This last, the rarest of the three forms described, may cause a diffuse cellular thickening of all the layers of the pyloric end of the stomach, and can readily be mistaken for a carcinoma. It may infiltrate the smaller curvature of the stomach, or may be confined to the pyloric end; for in syphilis, as in carcinoma and tuberculosis, the smaller curvature and the distal end of the stomach are the sites of predilection. Depending on the location of the lesion, the stomach may be small or dilated. Syphilis of the stomach has been found from the twenty-third to the seventy-third year; it may be hereditary or acquired; it occurs twice as often in men as in women; and when recognized surgically or on the postmortem table it is always of the tertiary type, whereas, when discovered clinically, it is usually of the secondary type. The disease may appear from the second to the fourth year after the primary lesion, though in hereditary lues the symptoms have been known to manifest themselves after a lapse of twenty-five years.

[6] Wien. med. Presse, 1902, xliii.

PATHOLOGY. The greatest number of cases described were of the acquired form, but they may also be of the hereditary type. Büttner[7] reports three cases in fœtal life, which, added to those already reported by Klebs, Cornil and Ranvier, Weichselbaum, Birch-Hirschfeld and Chiari, make only twelve cases in all.

In hereditary syphilis miliary gummas are found in the mucosa, submucosa, muscularis, and peritoneum. The vessels are narrowed and thickened, with here and there endarteritis obliterans. In the tissues themselves there are diffuse infiltrations, with necrosis and ulceration, but rarely complete perforation. In addition, embryonal tissue is frequently found. The acquired form of syphilitic gastritis manifests itself two to four years after the appearance of the chancre, and may appear pathologically as:

1. *Diffuse syphilitic gastritis*, with hyperemia and round-cell infiltration of all the layers of the stomach. It differs from ordinary gastritis in the greatly increased number of round cells in the submucosa and the formation of true gummas. Often, however, the pathological changes in the stomach are secondary to the morbid changes in the liver, pancreas, and small intestine. The gummas are the most characteristic growths found in gastric lues, and appear as more or less indurated plaques, or as vast zones of infiltration, going to the extent of a concomitant perigastritis. The number of these gummas is various; often they are exceedingly numerous, and they may vary in size from a few centimeters to the size of the palm of the hand. They are generally dirty white or yellow in color, rarely reddish, with hard, well-defined borders. Cross-section shows thickening of all the coats. Histologically, only the submucosa shows gummatous infiltration, while, as a result of the production of new tissue composed of embryonal cells and dense fibrous tissue, there is compression of the peptic glands and the usual luetic changes in the bloodvessels.

2. *Ulcers.* Syphilitic ulcers may exist alone or may be associated with gummas. Like simple peptic ulcers, they may be multiple, though they are usually solitary. They may be found anywhere, but the site of predilection is the posterior aspect of the cardia and the pylorus. They are usually round or oval, though occasionally irregular in form, and vary in depth from superficial erosions to complete perforation, either perforating rapidly into the free peritoneal cavity or more slowly with attendant perigastritis. Characteristic for this lesion are thickening of the mucosa and submucosa and nodules of infiltration followed by central necrosis, together with the constant finding of endarteritis and endophlebitis. The scars from healed syphilitic lesions are of doubtful value in a correct diagnosis, and are usually hard, white, and stellate.

In the earlier stages of these syphilitic lesions there is a tendency

[7] Prag. med. Woch., 1893, xviii.

to extend into the muscularis, the mucosa being affected much later. In the last stage of the development of the disease there is the usual obliterating arterial change found in all syphilitic lesions, thickening of the serosa with adhesions to the neighboring organs, and sometimes hyaline thrombosis with organization. Very commonly the ulcer extends deeply into the muscle, this being especially characteristic of syphilitic lesions everywhere.

3. *Tumors of syphilitic origin* are found but rarely in the literature and then only in postmortem records. In Einhorn's[8] cases, as in those that came under my own observation, all presented clinical characteristics of true carcinomas. There was progressive emaciation, together with all the other earmarks of malignant growth. Chemically, the stomach contents varied from the normal amount of free hydrochloric acid to complete absence thereof. Lactic acid was also absent, but there was present a considerable amount of sticky mucus streaked with blood. In the cases of syphilitic pyloric stenosis described by Einhorn, there was ischochymia coincident with the presence of a large, round, oval tumor at the pylorus. Two such cases came under his observation, and are probably the only ones which have been recognized clinically. Both of these cases improved under antisyphilitic treatment, though, as he rightly says, it may be seen readily that surgical intervention might have to be resorted to in order to correct the mechanical difficulty resulting from the syphilitic process.

I append the report of two cases of syphilitic tumors of the stomach which came under my personal observation:

CASE I.—An old lady of sixty years, greatly emaciated, with nothing special in her previous history except two or three miscarriages, presented herself in the clinic with distinct gastric symptoms. There was loss of appetite and occasional vomiting of sour masses; at times also particles of food that she had taken the day before. Upon examination, a hard nodular tumor was felt in the region of the pylorus, and a diagnosis of carcinoma made. The patient then disappeared from observation for at least several months, when, much to our astonishment, she reappeared, after we had long consigned her to the land beyond. On physical examination the plyoric tumor was unchanged, but it was now possible to feel over the right border of the liver a second tumor, hard, nodular, and similar in consistency to the first one described. On account of the history of her miscarriages, vigorous antiluetic treatment was instituted, and the patient rapidly improved, though when I last saw her the tumor had not materially decreased in dimensions, our experience in this respect not being similar to Einhorn's.

CASE II.—The second case was almost exactly like the first described, only the patient was a male. When I last saw him he was

[8] Archiv f. Verdauungskrankheiten, vi, 150.

in a fairly good physical condition, the antisyphilitic treatment which was instituted having had a pronouncedly favorable effect on his symptoms.

These two cases show us the importance of giving the patient the benefit of the doubt in all so-called inoperable cases of carcinoma by giving them strict antisyphilitic treatment, which can in no case do them any harm and may be of great benefit.

Symptoms. The symptoms of syphilitic gastritis are very diverse. They are commonest in the secondary stage and are due to a variety of causes. First and foremost, they may result from the general inanition and anemia attendant on syphilis, and, as in many other constitutional diseases, are not especially characteristic. We may have excretory or motor disturbances, with their attendant symptoms, such as hyperacidity, hypoacidity, and occasionally total absence of stomach secretions. Sometimes the stomach may fail to emply itself promptly, and in such cases there may even be intractable vomiting, approaching in severity gastric crises. Unlike the crises of tabes, however, these attacks readily yield to antiluetic treatment. In another class of cases the vomiting is somewhat less severe, but more persistent, resembling in some degree the vomiting of pregnancy. There is great variation in appetite, from complete anorexia to bulimia, attended by great thirst.

In tertiary syphilis, which is usually diagnosticated only at operation or on the postmortem table, the symptoms are very obscure. There may be, but rarely, the symptoms of acute gastritis, with its attendant pain, belching, and vomiting. Commoner is the chronic form of gastritis with pain and tenderness, the pain being commonly more severe at night, irregular vomiting, anorexia, associated with diarrhœa and meteorism—symptoms refractory under ordinary treatment, but readily controlled by specific treatment.

More important is syphilitic gastric ulcer, which differs clinically in no wise from ordinary peptic ulcer except in its peculiar intractability to all ordinary medical treatment, though it is more easily controlled if to the usual procedure of diet and rest are added the antiluetic treatment. Syphilitic ulcers may, for purposes of clinical description, be divided into three groups: (1) Those which are preceded by stomach trouble, without anything especially characteristic about them; (2) the acute variety, like the ordinary round ulcer; (3) those which first run a latent course, and then suddenly manifest themselves by an alarming hemorrhage.

The prognosis naturally depends upon an early recognition of the condition, some cases running a fulminating course.

In syphilitic ulcer of the stomach there may be pain about the ensiform, radiating through to the back, hematemesis, melena, etc. Fournier,[9] for example, tells of a stomach hemorrhage in a woman

[9] Klin.-therap. Woch., 1900, vii.

who had acquired lues six years previously, and who recovered completely after antisyphilitic treatment was instituted. Flexner[10] reports an undoubted case of perforating syphilitic stomach ulcer. Mackay[11] reports a syphilitic ulcer with hematemesis in a young man, suffering from hereditary lues, who was greatly benefited by the use of mercury and the iodides.

Einhorn, unlike Fraenkel, believes that stomach syphilis is not a rare condition. He reports three kinds of cases: (*a*) Ulcers on a luetic basis; (*b*) syphilitic tumor of the stomach; (*c*) syphilitic pyloric stenosis; and he cites a number of cases in support of his views.

Gaillard[12] also concludes that stomach syphilis is not as rare as had been previously supposed, and wonders why it is not as reasonable to attribute ulcerations lower down in the intestinal tract to the same cause (namely, syphilis) as those which attack the buccal mucous membrane and pharynx; in support of his views he cites a number of authors to support his contention, such as Andral, Hayem,[13] and others, who have successfully cured obscure dyspepsias with mercury and the iodides. Anatomically, gastric scars in syphilis have been found by Frerichs, Chvostek, and others; and gummas by Klebs and Carril; while simple round perforating ulcers in luetic individuals have been described by Murchison and Fraupé. The last-named author comes to the following very necessary conclusions: (*a*) That gastric syphilis is not as rare as has been supposed; (*b*) that there are three anatomical lesions of a syphilitic character; (*c*) that the treatment bears out the suspicions of the luetic basis of many obscure stomach lesions.

L. Gaillard's views of syphilitic stomach disease are embodied in the following pathological summary: (*A*) Hereditary lues, in which are found miliary gummas, first in the mucosa and submucosa; later, in the muscles of the peritoneum, with obliterating endarteritis. Diffuse infiltrations, with the formation of embryonal tissues. Necrosis and softening of the syphiloma. Ulcerations are frequent, perforations exceptional. (*B*) Acquired syphilis, with morbid findings, such as have already been discussed.

Here I refer to a number of cases of stomach syphilis reported by Hayem, Morgan,[14] Hoover, Hemmeter and Stokes,[15] which are exceedingly interesting, but of which, for the sake of brevity, I must omit more detailed mention. Nor can I in the space allotted me do more than refer to gastric cirrhosis following syphilis, which has received considerable attention from French authors; nor shall I

[10] Amer. Jour. Med. Sci,, 1899, n. s., vol. cxvi.
[11] Lancet, London, 1898, vol. ii; Syph., Paris, 1903, vol. i.
[12] Presse méd., Paris, 1897.
[13] Ibid., 1906, vol. xiv; Rev. de Méd., Paris, 1889, vol. ix.
[14] American Medicine, Philadelph a, 1906, n. s., vol i
[15] Johns Hopkins Hospital Reports, 1900, vol. ix.

enlarge upon the interesting case reported by Lafleur,[16] which was exceedingly suggestive of malignancy until microscopic examination proved it to be specific.

SYPHILIS OF THE INTESTINE. In Büttner's cases of congenital syphilis of the stomach there was, as already stated, syphilis of the small intestine. Hayem and Tissier report similarly in reference to a case of syphilis in which the patient, a woman journalist, aged thirty-three years, was admitted to the hospital. She gave a history of having what was called scrofula and hemiplegia, which, however, lasted only two months. She was now admitted to the hospital in a typhoid state, presenting on examination a papulosquamous syphiloderm. She died on the fourth day, and at the autopsy numerous ulcers in the cecum and colon, of various dimensions, irregular and round were found. The borders were indurated, the base whitish, covered with a purulent exudate, and surrounded by a reddish areola. Microscopically, there was found infiltration of all the layers, with congestion of the vessels, which also showed an end- and peri-artertitis.

Hueter[17] reports the following case of a woman, aged forty-four years, who for the past four years had enlarged inguinal glands and obstinate diarrhœa. Death resulted from intercurrent pneumonia. At the postmortem there was found, in addition to lues of the rectum and arch of the aorta, multiple ulcerations in the lower ileum, with corresponding constrictions and ampulla-like dilatations between the strictures. The distinguishing features which speak for lues of the intestine are: multiplicity of the lesions collected in groups, the tendency to ring-like formation, and plaque-like infiltration, all of which were present in this case.

Similarly, Gutman[18] reports a case with autopsy findings, and gives general conclusions thereto. A woman, aged forty years, was admitted to the hospital suffering from diarrhœa and great loss of weight. She had had no abortions, and her history was negative as to alcoholic excess, lues, or tuberculosis. On the day of admission she had chills, accompanied by fever, which continued, with remissions, until seven weeks later, when she died of pneumonia. No tubercle bacilli were found in the sputum or feces. At the autopsy, after the omentum was uncovered, the small intestine from the jejunum down presented a number of annular constrictions, with dilatation of the gut between them. The peritoneum over these places was thickened, as was also the mesentery. On opening the bowel, it was found that the annular constrictions described corresponded to ulcers on the mucosa. The ulcers were flat, the edges undermined here and there, the base smooth, bluish red or yellow, and firm to the touch. No nodules were found.

[16] Montreal Medical Journal, 1903, vol. xxxii.
[17] Münch. med. Woch., 1906, vol. liii.
[18] Deut. med. Woch.,1903, vol. xxix.

Microscopically, the floor of the ulcer was found to be formed of the submucosa, which was infiltrated with round or polygonal cells, invading the muscularis and serosa, and extending to the mesentery. No tubercles or giant cells were found, though obliterating endarteritis was present.

The case of syphilis of the intestines which came under my own observation follows: The patient, a male, aged thirty-eight years, had always been well, except for syphilis acquired fifteen years previously. During the last three years before consulting me he suffered from intractable diarrhœa, with fourteen or fifteen bowel movements daily. The stools were thin and watery, with an admixture of blood and pus. Neither the rectoscope nor sigmoidoscope showed the presence of an ulcer; however, upon deep palpation over the sigmoid, exquisite tenderness was elicited. From this fact, and on account of the previous luetic history, a tentative diagnosis of syphilitic ulcer of the bowel was made and a vigorous antisyphilitic treatment instituted, intravenous injections of 1 per cent. bichloride of mercury being given. Within a very short time the diarrhœa stopped, the stools became formed, and their number reduced to one daily, in spite of a liberal mixed diet.

From the history and results of treatment, we may add this case to those already enumerated, although we have no anatomical findings to support our diagnosis. Such cases may run with a low continued fever, reminding one somewhat of typhoid, and are often very puzzling. If, however, we take into consideration the fact that the pathological anatomists have shown that syphilis may cause retracting and radiating scars of the intestine, besides involvement of the bloodvessels in an obliterative endarteritis, there is no reason why we cannot look upon syphilitic enteritis as a clinical entity, in which the symptoms may be due either primarily to the syphilitic toxin, or secondarily to the anatomical changes of syphilis.

Fournier was the first to call attention to the existence of a febrile affection like typhoid fever due to syphilis of the intestine. He sees no reason why the luetic virus, attacking every other organ, should not as well affect the intestine. The addition of scars, retracted and radiating, involvement of the peritoneum and bloodvessels, establish the contention that syphilis of the gastro-intestinal tract is not a clinical curiosity, but a well-defined condition with characteristic lesions.

Homen[19] reports a case of a man, aged twenty-three years, who for many years had gastro-intestinal trouble. He gave a direct luetic history, for which he was treated, with apparently fair recovery. Later, however, he commenced to have nocturnal abdominal pains, diarrhœa alternating with constipation, bloody stools, and abdominal distention. He died of an influenzal pneumonia. At autopsy

[19] Central. f. allg. Path. u. pathol. Anat., Jena, 1893, iv.

the small intestine was found to have been constricted in thirty different places by scars, 1 cm. wide, and circularly disposed. Over the mucosa there were over thirty ulcers with smooth bases and thickened edges. The submucosa was greatly infiltrated.

CONCLUSIONS. The diagnosis of stomach syphilis can be considered probable if, with luetic history and specific scars, there are found at the same time gummatous infiltrations. The hemorrhages can most easily be explained by concomitant portal obstruction. Clinically, the fact must not be lost sight of that in luetic subjects who have been overdosed with iodides and mercury there are often profound digestive disturbances, and that these disturbances must in no wise be confused with gastric lues, for in gastric syphilis the stomach symptoms improve under specific therapy, whereas the first named are aggravated by Hg and KI.

The conclusions drawn by Reder as regards lues of the small intestine are: (1) Ulcers are found in the entire small gut, especially in the lower jejunum; (2) they always occur in groups, and the number thereof may be very great; (3) they are always annular, and the floor is deep and smooth; (4) they always produce stenosis; (5) they are all similar histologically; and (6) the lesion begins with a new cellular infiltration, surrounding the vessels especially.

TREATMENT OF SYPHILIS OF THE STOMACH. From the foregoing it will be readily seen that when there is suspicion of a syphilitic etiology for otherwise obscure stomach trouble, we must proceed with the greatest caution in instituting antisyphilitic treatment. It must not be forgotten that this disease causes profound pathological changes in the stomach itself, and that for this reason the use of the specific treatment usually employed will not be sufficient to remedy the disease. To begin with, the iodides and mercury, if their use is determined upon, must be given in such a form as not to cause further irritation to the stomach. The mercury should therefore not be given by the mouth; it is best exhibited in intravenous injections—as 1 per cent. bichloride of mercury in a dosage of 0.5 to 1 c.c., given three or four times a week. The iodides are particularly obnoxious to a sensitive stomach, and should either be given per rectum, in the proper dosage, or, if given by the mouth, should be well diluted; moreover, it has been found that the sodium salt is less irritating to the stomach than the potassium. Mercury may also be given in the form of inunctions. The inunctions should be given six days in succession, and on the day on which they are omitted it is well to advise a Turkish bath. Mercury may also be given intramuscularly, with the usual precautions, and for this purpose a 2 per cent. oxycyanide may be chosen. In addition, as before indicated, the diet should be carefully regulated, as it would be in any other corresponding stomach disease. If there are hemorrhages, the patient should be put at rest in bed with rectal feeding, and if surgical complications arise, they should be treated as any other

surgical complications would be, irrespective of the syphilis. A constricting tumor of the pylorus, for example, if followed by dilatation of the stomach and intractable vomiting, which does not yield to syphilitic medication alone, should be excised or a gastroenterostomy should be performed, even though syphilitic subjects are, as a rule, poor surgical subjects. Yet in these cases we should not hesitate any more than we would in cases of diabetes, when the indications are to save life, even in spite of the diabetes. When once the stomach symptoms have abated, the patient should be given to understand that repeated antisyphilitic cures are necessary, in order to avoid constitutional symptoms in the future.

THE LIVER IN TUBERCULOSIS.

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The liver in tuberculosis has been studied by a number of observers in the course of the last century. By the earlier observers it was thought to be only rarely the seat of tubercles or other manifestation of the general disease, but with the improvement of the microscope and histological methods, we find that very few cases of tuberculosis go to autopsy without some evidence of the disease in the liver.

Louis,[1] in 1843, found tuberculosis of the liver but twice in 120 autopsies on tuberculous subjects. Forster,[2] in 1854, was able, after a prolonged search, to find but three cases of hepatic tuberculosis. In an investigation undertaken by Bristowe,[3] in 1858, to discover the relation between liver abscess and intestinal ulceration, he found that of 167 cases of tuberculous ulcers of the intestine, but 17 showed "tuberculous cavities of the liver." Waldenberg,[4] in 1869, reported that it is the organ most frequently affected in experimental tuberculosis, but this is due to inoculation into the peritoneal cavity. Arnold,[5] in 1880, considered it an almost constant finding in cases of tuberculosis. Simmonds,[6] in 1888, found it in 76 per cent. in adults, in 92 per cent. in children, and in 78 per cent. in general. Zehden,[7] in 1897, found miliary tubercles in 50 per cent. of fatal cases, corresponding with the frequency of intestinal ulceration. Rolleston[8] is inclined to put it at a lower figure than 50 per cent. Rosenberger,[9]

[1] Recherches sur la phthisie, Paris, 1843.
[2] Handb. der spec. path. Anat., 1854.
[3] Trans. Brit. Path. Soc., 1858, ix, 241.
[4] Die Tuberculose, Berlin, 1869.
[5] Virchow's Archiv, 1880, Band. lxxxii.
[6] Deut. Archiv für klin. Med., 1888.
[7] Cntrlbl. für path. Anat., 1897, viii.
[8] Diseases of the Liver.
[9] Trans. Phila. Path. Soc., 1906, ix.

in 1906, found miliary tubercles in 83.8 per cent. of livers examined histologically, and White,[10] in 1907, found them in 70.3 per cent.

Tuberculosis manifests itself in the liver as: (1) Miliary tubercles; (2) solitary tubercles; and (3) tuberculous cirrhosis.

I. MILIARY TUBERCLES. Miliary tubercles are decidedly the most common manifestation of tuberculosis in the liver, and have been described by many observers. They are usually found either in or adjoining the portal spaces, but may be found within the lobule. It is thought by most men that the infection comes from ulcers of the intestine by way of the portal vein, and that the lesion is located in the portal spaces for that reason.

Infection of the liver may take place in utero, the bacilli being transmitted by the umbilical vein. Sabourad,[11] in 1891, found miliary tubercles of the liver and spleen in a child eleven days old, in whose mother there was phthisis pulmonalis, but no genital or mammary tuberculosis. He concluded that the infection travelled by way of the umbilical vein. Nocard,[12] in 1895, reported a case of tuberculosis of the liver in a calf, in whose mother's placental cotyledons there were tubercles containing giant cells. Von Honl[13] found tubercles in the liver and other organs of a fifteen-day-old child in whom the tubercles undoubtedly antedated birth. His reason for believing that they were older than fifteen days was the amount of fibrous tissue about the lesions. D'Arrigo[14] inoculated female guinea-pigs with tuberculosis, and then allowed them to become pregnant. Some went to term and others aborted. In those going to term the offspring showed tubercles, particularly of the abdominal organs. In those aborting after the first half of pregnancy there were tubercles and tubercle bacilli in the livers of the offspring. Bar and Renon[15] inoculated into animals the blood from the cut umbilical cord of children born of tuberculous mothers. In two cases out of five the animals showed tuberculosis. In one case the child died, and portions of its organs were inoculated into animals and produced tuberculosis in the animals. From the observations of these authors we conclude that tuberculosis can be carried from mother to child by way of the umbilical vein, and that it usually manifests itself in the liver.

In the adult the infection is generally considered to take place by way of the portal vein. Rolleston thinks that the infection takes place by way of the portal vein in chronic tuberculosis, and by way of the hepatic artery in acute tuberculosis. This view is also held by Zehden, who thinks that the initial foci are apt to be in the intermediate zone of the acini, where the lumen of the vessels is the

[10] Third Annual Report, Henry Phipps Institute, 1907.

[11] Semaine méd., 1891, No. 85.

[12] Revue de la Tuberculose, 1895.

[13] Acad. des sciences de l'Empereur Franz Joseph I, Bulletin International, Prague, 1895.

[14] Cntrlbl. für Bakt., 1900.

[15] Soc. de biologie, June 29, 1895.

narrowest. Orth[16] thinks that the infection travels from the portal vein by way of the lymph channels. Kotlar[17] made very careful examinations of the liver histologically and bacteriologically, and came to the conclusion that the infection was hematogenous and not via the bile ducts. Lancereaux[18] thinks that it comes from the intestine by way of the portal vein. Klebs[19] thinks with Zehden that the infection starts in the intermediate zone and spreads peripherally via the lymph channels. Gibbert and Lion[20] produced tuberculosis of the liver experimentally by injecting tubercle bacilli into the portal vein. The tubercles were found partially in the portal spaces and partially in the lobules.

Histological examination of 100 livers was made by us. The blocks were cut as for the routine histological work, no special care being taken to pick out pieces that seemed to contain tubercles. Of the 100 livers, miliary tubercles were found 79 times. Some of these lacked the giant cell, but the other characteristics were present, and we had no hesitancy in calling them tubercles. Seventy-four livers were stained for tubercle bacilli, with a positive result in 28, a percentage of 37.9. The infrequency with which tubercle bacilli are found in the liver has been commented upon by a number of observers, notably Baumgarten,[21] Brissard and Loupet,[22] Hanot and Lauth,[23] and Koeckel,[24] and we found that they are extremely hard to demonstrate. In two cases of acute miliary tuberculosis we found them in large numbers, but in all the rest we could only find a few, and then after a prolonged search.

The position of the tubercles was periportal 40 times, intracinal 17 times, and both periportal and intracinal 22 times. In a series of 45 examined particularly with reference to intestinal ulceration, the ulcers were found 38 times. Of these 38, the lesion in the liver was periportal 26 times, in 3 the lesion was intracinal, and in 9 the lesions were both periportal and intracinal. In the 7 cases showing no ulcers in the intestine, there were periportal tubercles in 2, intracinal in 3, and both periportal and intracinal in 4 cases. It seems likely from the findings in these cases that the infection generally comes from the intestine via the portal vein, but that in all probability it does come also from the general circulation by way of the hepatic artery. In two cases of acute miliary tuberculosis the tubercles were found in the portal spaces and also scattered throughout the parenchyma, and it is probable, as asserted by Zehden, that the infection in acute tuberculosis comes by way of the hepatic artery.

[16] Virchow's Archiv, 1871, Band lxvi.
[17] Ztsch. für Heil., 1894, iv.
[18] Traité dès Maladiès des Foie et du Pancréas, 1899, 662.
[19] Allg. Path., 1869.
[20] Société de biologie, 1888.
[21] Ztschr. für klin. Med., Band ix, x.
[22] Études Exp., Sous la direct. du Prof. Verneuil, I, Paris, 1887.
[23] Ibid., II, Paris, 1888.
[24] Virchow's Archiv, 1896, Band cxliii.

II. SOLITARY TUBERCLE. Under this heading we include all the large caseous masses occurring in the liver, whether single or multiple. This is a very constant finding in the liver of many of the lower animals, particularly birds, where it is the only organ attacked in 20 per cent. According to Hutchinson,[25] tuberculosis of the liver was absent but twice in a series of 25 cases of avian tuberculosis. It occurs also very often in the liver of monkeys and cattle. Under this heading there are two subdivisions: (1) Conglomerate tubercles, and (2) tuberculous cavities or bile duct tubercles.

By *conglomerate tubercles* is meant the collection of large caseous masses which are found scattered throughout the liver substance. Craven Moore[26] reports a case of conglomerate tubercles in the liver in a case of cancer of the stomach, and thinks that the infection came from the ulcerated surface in the stomach. Orth reported two cases, but it was before the discovery of the tubercle bacillus, and the diagnosis was disputed by Zehden and Simmonds,[27] who think he had to do with either a gumma or a cancer. Other cases are reported by Simmonds, Rolleston, MacKenzie,[28] Anderson,[29] Middleton,[30] and Clement.[31] The centres of the nodules may undergo softening, in which event we may have the appearance of a cavity with caseating walls.

The *bile duct tubercles* are so called because of their association with the bile ducts, and it was claimed by Virchow that the ducts were occluded by tubercles and cysts formed. It has also been thought that the infection came from the intestine by way of the bile duct. Both these theories seem to be in error. Instead of the bile duct being occluded, it is likely that the tubercle caseates and breaks down, leaving a caseating cavity, which communicates with a bile-duct by extension and is oftentimes blood-or bile-stained, and this has given rise to the idea that the bile duct is occluded and forms a cyst.

As to the source of the infection, it has been claimed by Simmonds that it came by the bile duct, but Sargent,[32] Kotlar, and Sabourin[33] think that it comes by the portal vein or the hepatic artery, and that the duct is only secondarily involved by extension, the tubercle breaking into the duct and infecting it, and in this way producing other tubercles. Cases are reported by Simmonds, Hare,[34] Wethered,[35] and MacKenzie. In our series we have one case showing solitary

[25] Studies in Human and Comparative Pathology, p. 304.
[26] Medical Chronicle, October, 1889.
[27] Centralblatt für allgemeine Path., November, 1898.
[28] Transactions Path. Soc., xli, 146.
[29] The Australian Medical Gazette, March 20, 1899.
[30] Glasgow Journal, February, 1893.
[31] Virchow's Archiv, vol. cxxxix.
[32] Thèse de Paris, 1895.
[33] Le foie des tuberculeux, Archiv. de physiol. norm. et path. le 1er Juillet, 1883.
[34] Transactions London Path. Soc., 1858.
[35] Ibid., 1889.

tubercles associated with miliary tubercles. The lesions averaged about 1.5 cm. in diameter, there was a number present, but there was no cavity formation.

Cirrhosis. Cirrhosis of the liver may accompany tuberculosis and be due to an entirely different cause. For instance, we may have an alcoholic cirrhosis, superimposed upon a tuberculous infection. We may also have cirrhosis of the liver with tuberculosis elsewhere in the body, but it has long been felt that there is a fibrous hepatitis due to the tubercle bacillus. Briege, in 1879, described a fibrous hepatitis occurring in tuberculous patients, with the formation of fibrous tissue which enclosed the lobules, together with the newly formed bile ducts. Rolleston discusses at some length cirrhosis of the liver associated with tuberculosis. He quotes Hanot and Gilbert, who describe a large fatty liver with a small-cell infiltration and fibrous hyperplasia of the portal spaces, together with miliary tubercles. This they call "hypertrophic fatty tuberculous hepatitis."

These authors describe two other forms: (*a*) Cirrhosis without any enlargement of the liver; (*b*) cirrhosis with more fibrous tissue than the variety just mentioned, but with similar fatty change and tuberculous infiltration. The two latter forms differ only in the fact that one shows marked nodules, like those seen in cirrhosis with adenomas. Rolleston thinks that these forms occur, but he does not think them tuberculous. He considers it reasonable to suppose that the tubercle bacillus is capable of a sclerogenic effect on the liver. In animals, as in guinea-pigs, Hanot and Gilbert were able to produce a cirrhosis of the liver by the injection of avian tubercle bacilli, while human tubercle bacilli produced fatty change or fatty coagulation necrosis. Hanot found a deeply scarred liver, like that of acquired syphilis, associated with miliary tubercles in the organ. Collet and Gallivardin, according to Rolleston, report a case of tuberculosis of the portal spaces with a delicate fibrosis accompanying. Mixed infection, according to Rolleston, may set up a gastritis and a consequent dyspeptic type of cirrhosis. A marked grade of passive congestion may set up a cirrhosis—the so-called cardiac cirrhosis.

In this series one case of atrophic cirrhosis was found, and newly formed bile ducts and a slight increase of fibrous tissue several times; but the data are insufficient to warrant a conclusion that the tubercle bacillus is an etiological factor in these changes.

Coincident Pathological Processes. *Amyloid Degeneration.* This is a more or less frequent occurrence in chronic tuberculosis, not only of the lungs, but also of the bones. In this series it was found ten times, or 10 per cent.

Fatty change in the liver has been the subject of much discussion. Langerhans thinks that it is due to paralysis of the hepatic cells, and that the fat physiologically stored there is not given up. Klebs

thinks that it is the direct result of the tuberculous process on the lymphatic apparatus of the liver, the lymph outflow being hindered and the fat retained. In our series it was present in 35 cases, or 35 per cent.

Congestion. The occurrence of congestion in the liver is, of course, not characteristic of this disease, and yet it is an almost constant finding. In chronic lung disease the embarassed respiratory apparatus, with its effect upon the right heart, sooner or later gives rise to passive congestion. The liver, with its close proximity and its blood supply, is one of the first organs to show the change. In our cases we classified the congestion as slight, moderate, and severe. There were 25 cases of slight congestion, 47 of moderate, and 22 of severe. In 6 cases congestion was not present.

Conclusions. 1. Miliary tubercles are found in the great majority of the livers of the cases of chronic phthisis autopsied.

2. Solitary tubercle of the liver is a very rare manifestation.

3. The infection probably is hematogenous, the bacilli being carried to the liver by the portal vein and the hepatic artery. In most cases the infection arises in intestinal ulcers.

4. Passive congestion of the liver is found in nearly every case of pulmonary tuberculosis, while amyloid and fatty change are found in a relatively small number of cases.

5. From our cases we are not convinced that a fibrosis or cirrhosis of the liver due to the tubercle bacilli does occur, and are more inclined to think that the fibroses found are due to other etiological factors.

My thanks are due to Dr. C. Y. White for the material on which this report is based.

ASCITES IN CIRRHOSIS OF THE LIVER CURED BY REPEATED TAPPINGS.

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In a paper widely read and frequently quoted, Hale White[1] has expressed himself in very pessimistic terms concerning ascites in cirrhosis. In studying the records of Guy's Hospital for five years, the works of Frerichs[2] and Murchison,[3] and a paper of Dr. F. Taylor,[4] he was unable to find a single patient with ascites due

[1] Guy's Hospital Reports, 1893, xlix, 1.
[2] A Clinical Treatise on Diseases of the Liver. The Sydenham Society, London, 1861.
[3] Diseases of the Liver, 1867.
[4] Guy's Hospital Reports, xxxvi.

to uncomplicated cirrhosis who had lived long enough for a second paracentesis. He insists that a patient with alcoholic cirrhosis and ascites has not long to live. At the opening of his paper he says: "Another point which I shall try to prove is, that if a patient, who during life is supposed to be suffering from cirrhosis of the liver with ascites, has the abdomen tapped, but life is sufficiently prolonged to allow a second paracentesis to be necessary, the diagnosis of cirrhosis of the liver is almost certainly completely wrong, or, at any rate, the patient has something else the matter in addition to his cirrhosis, and further, it is highly probable that he has some form of chronic peritonitis, of which what is ordinarily called perihepatitis is merely a variety." Although written fifteen years ago, and although Hale White's principal objection to the cure of ascites in cirrhosis has been removed by autopsy experience, his paper in its main contention that many alleged cirrhotics are suffering from some entirely different disease holds perfectly good today. In mentioning some recorded cases of cured ascites in cirrhosis, Quincke and Hoppe-Seyler[5] remark: "When in uncomplicated cirrhosis ascites once develops, it disappears only exceptionally." Hilton Fagge[6] stated his belief that death in cirrhosis occurs from six weeks to six months after the detection of ascites, although he admitted the possibility of cure.

In view of the acknowledged rarity of the event under consideration, the following case report is perhaps not inappropriate:

History 5762, new series. Male, aged fifty-eight years, Italian, married, car cleaner; admitted to the Vanderbilt Clinic, October 9, 1907.

His mother and father died of old age. He does not remember having had the diseases of childhood nor any other acute disease; denies all venereal infection. Up to five months previous to admission he drank very heavily, and was in the habit of taking ten to twenty "whiskies" daily, often some before breakfast. He was also in the habit of consuming much beer and wine. His misuse of alcohol existed over many years. Six months previous to admission the patient noticed that his feet and shins began to swell, and two months later that his abdomen was becoming larger. Within a month the belly became so large that paracentesis was performed, and five and one-quarter gallons of amber-colored fluid was withdrawn. A month later a second aspiration was made, and four and one-half gallons was removed. A third tapping was made two weeks previous to admission, and the patient says an indefinite amount of fluid was obtained, and some blood came away in addition. Since the last aspiration the abdomen has become rapidly larger, and causes much discomfort; he is obliged to get up two or three

[5] Krankheiten der Leber, Nothnagel, Spec. Path. und Therap., 1899, p. 381.
[6] Guy's Hospital Reports, 1875, Third Series, xx, 155.

times at night to urinate. He has had some gastric discomfort, but no vomiting nor hematemesis. He has had no tarry stools. He has become much thinner about the face and limbs, has lost much strength, and feels very weak and ill. He has had no fever, no cough. His appetite is fair and his bowels are regular.

Examination showed the patient to be poorly nourished. The heart was slightly enlarged to the left; but otherwise negative. The pulse was 108, regular, and rather weak; there was moderate thickening of the radials. The lungs were negative. The abdomen was large and pendulous; the superficial veins were visible. There was movable dulness and a fluid wave. The liver and spleen could not be made out on account of fluid in the belly. There was moderate œdema of the shins. The urine contained a moderately heavy trace of albumin.

On October 14 the abdomen was aspirated at the patient's home, twenty-one quarts of clear serum being obtained. On October 21 the patient was admitted to the Roosevelt Hospital at his own request. He was aspirated once in the hospital. On November 19 the abdomen was aspirated, and twenty-five quarts was obtained. On December 3 twenty quarts were obtained, and on January 4 twelve quarts; the œdema of the abdomen, etc., had gone. On January 28 the circumference of the abdomen was forty-four inches. The urine was smoky and had a red sediment, contained a marked trace of albumin, but no sugar; a few hyaline casts, much blood, urobilinogen were present. On March 6 the patient said he felt well; the circumference of the abdomen was forty-one and one-half inches. The liver-edge could be felt four and one-half inches below the free margin of the ribs in the nipple line (it was never felt before). The spleen was felt for the first time, one and one-half inches below the left free costal margin. On May 21 the circumference of the abdomen was forty-one inches. The patient felt perfectly well and returned to work. On October 30 the patient had grown fat, was very active, and felt entirely well. He had returned to his excessive alcoholism. Spider angioma and dilated venules of the face had appeared. The liver and spleen were palpable. There were no signs of fluid. The circumference of the abdomen was forty-one and one-quarter inches.

Syphilis of the liver was suggested, and the possibility of the cure being due to antisyphilitic treatment was discussed. As the patient gave no history and showed no traces of that disease, as the liver when finally palpable presented none of the physical features so characteristic of syphilis of that organ, and as the antisyphilitic treatment amounted to only a few drams of potassium iodide over the entire period of observation, it seemed that hepatic syphilis did not merit serious consideration.

The question arose whether cardiac insufficiency was operative in producing the ascites. The history states that the first objective

deviation from normal health was swelling of the legs, a manifestation not ordinarily referable to portal obstruction. Frerichs has stated that too much importance must not be placed in the appearance of ascites before œdema of the feet, for, as he points out, in some cases of cirrhosis ascites and œdema of the lower extremities come on together. It is possible that in the case here reported the accumulation of fluid in the abdomen escaped the patient's notice for some time. While under observation the most rapid accumulation of ascitic fluid seemed to be coincident with the greatest degree of œdema of the legs and scrotum, and it is a fact of some significance that he was given the infusion of digitalis for a long time. Consequently, it seemed probable that the ascites was due in this case to an intrahepatic portal obstruction in an individual whose systemic circulation was not altogether adequate.

The patient died March 17, 1909, after having had the symptoms of intestinal obstruction for one week, probably due to a strangulated umbilical hernia. Permission was granted to make a small incision in the abdominal wall. About a quart of fluid was found in the peritoneal cavity, probably incident to the condition from which he died. The transverse mesocolon was adherent to the abdominal wall from the ensiform cartilage to the ninth right cartilage, and to the liver below and to the right of that point. The adhesions were not dense, nor highly vascularized. The liver was adherent to the diaphragm by a very few readily broken adhesions, was greatly diminished in size, and showed the lesions of advanced cirrhosis. There was no perihepatitis. The peritoneum, as far as could be seen, showed no evidence of acute or chronic inflammation.

A review of the literature furnishes a few examples of ascites in cirrhosis cured by tapping. MacDonald[7] has had two cases of ascites in cirrhosis cured by tapping. An intemperate butcher, aged forty-eight years, who was aspirated twenty-one times over a period of nine months, was back at work, without ascites and feeling perfectly well, eight months after the last paracentesis. Another patient, admitted to the Montreal General Hospital in August, 1885, after sixty tappings, was cured of ascites, and four years after the last operation had had no return. Cheadle[8] gives the history of a very alcoholic woman who was tapped twice. Fluid did not return, the patient gained weight and left the hospital. Nine months later she had to be aspirated a third time. She went through a pleuropneumonia, and although in an apparently hopeless condition recovered. Two months later she succumbed to an acute bronchitis. The postmortem "disclosed a contracted, typically hobnailed, cirrhotic liver, weighing thirty-eight ounces, with thickened capsule, but no general perihepatitis or peritonitis, and no thickening of or

[7] Med. News, 1889, lv, 398.

[8] Lancet, 1900, i, 987.

adhesion to neighboring structures." Cheadle also details the case of a cabman, aged forty-three years, of very intemperate habits, who was tapped nineteen times between April and August, 1894, the last aspiration being August 19. In August, 1895, he was re-admitted for hematemesis, from which he died. The liver was contracted, markedly hobnailed, weighed forty-eight ounces, and was covered by a "thick false membrane." There was no general peritonitis. H. P. Hawkins[9] mentions an alcoholic who came under Murchison's care for cirrhosis and ascites. He became a total abstainer, lived twelve years without ascites, and died of granular kidneys and peritonitis. Autopsy showed a hobnail liver. In Casati's[10] case, a cirrhotic with parenchymatous nephritis and diabetes mellitus recovered after one hundred and eleven aspirations.

In a series of 56 hospital cases, over a period of twenty years, Saundby[11] has contributed 3 cases in which the ascites incident to cirrhosis disappeared after a number of tappings. Case III was tapped four times in five years and then had no return. Case LV was tapped twice, lived comfortably for three years, and then died by accident. Case LXVIII was tapped five times between June and October, 1901, and had no return of ascites up to the time of writing in 1905. Grasty's[12] case required twenty-one tappings in thirteen months, and at the time of reporting had been free from ascites for two years. Courmont[13] has contributed one case of ascites, cured b a salt-free diet. Bristowe[14] has recorded 3 cases of ascites in cirrhosis which have been cured. Hale White, while admitting that these cases present very strong evidence of the curability of the condition, objected that there had been no autopsies to prove it. The objection, however, has since been weakened by the cases of Cheadle and Hawkins.

The disappearance of ascites is generally supposed to result from the development of a collateral anastomosis between the portal vein and the venæ cavæ, by paths too well known to warrant description at present. Admitting that such a communication is essential to the cure of peritoneal dropsy, it seems that other elements are involved in the process.

A consideration of certain observations, fairly common in the experience of medical men, may aid to an approximately accurate understanding of the disappearance of ascites in some cases of portal cirrhosis:

1. Ascites is sometimes observed when the only demonstrable lesion in the liver is chronic passive congestion resulting from

[9] Allbutt's System of Medicine, 1908, iv, Part 1, 180.
[10] Il racoglitore medico, 1893, Fifth Series, xvi, 161.
[11] Practitioner, London, 1905, lxxiv, 758.
[12] The George Washington Bulletin, 1906, v, 45.
[13] Bull de la soc. méd. des hôp. de Lyon, 1904, iii, 48.
[14] Brit. Med. Jour., 1892, i, 847.

cardiac insufficiency with or without valvular disease. Hart[15] has examined 35 cases of "high grade, central, red atrophy," occurring in adhesive pericarditis, valvular and muscular disease of the heart. Normal livers were used as controls. The microscope showed dilatation of the central veins and capillaries. The liver cells were normal or diminished in size toward the periphery of the lobule, but toward the central vein the diminution became more marked, the cells appearing atrophied. The protoplasm in this situation limited itself to a small rim, until in the centre of the lobule only nuclei and their fragments were to be found. In the capillaries coagula were found which proved to be fibrin, and Hart concluded they were formed antemortem. Hale White has drawn attention to the rapid accumulation of fluid in some cases, and considers it difficult of explanation if compression of the portal radicals by slowly forming connective tissue is to be regarded as the sole cause of ascites. He suggests that rapidly accumulating ascites "is due to thrombosis of some of the minute branches of the portal vein within the liver."

2. After more or less prolonged alcoholic excess, cases of œdema of the lower extremities are occasionally seen, without abnormal signs in the heart and without albuminuria. Rest and removal of alcohol suffice to cure the œdema.

3. In a certain number of alcoholics, the liver is found to be distinctly enlarged. After alcohol has been withrawn for a number of weeks, the edge of the liver is not as far below the costal margin as previously, and, indeed, in some cases is no longer felt. Quincke and Hoppe-Seyler speak of an enlargement of the liver in persons who subsequently become cirrhotic, probably due less to connective tissue than "to fat infiltration and congestion."

4. In some cases of cirrhosis, the disappearance of ascites seems to be coincident with the cessation of alcoholism. This was a notable feature in the case of Hawkins.

In view of these clinical and pathological facts, apparently indicating the ability of alcohol to depress the circulation and directly or indirectly to induce hepatic hyperemia, and in view of the fact that in the case here reported œdema existed which cannot be altogether explained by portal obstruction, an improvement of systemic circulation—in this case at least—seems a likely factor in the cure of ascites in cirrhosis.

[15] Beit. zur path. Anat. u. z. allg. Path., 1904, xxxv, 303.

ADIPOSIS DOLOROSA.

A CLINICAL AND PATHOLOGICAL STUDY, WITH THE REPORT OF TWO CASES WITH NECROPSY.

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The number of cases of adiposis dolorosa that have been recorded with postmortem findings is so few that the following should be of interest:

Case I.—M. F., a housewife, white, aged fifty-seven years, a native of Philadelphia, was admitted to the alcoholic ward of the Philadelphia General Hospital, November 11, 1907, under the care of Dr. Mills; subsequently she was transferred to the service of Dr. Dercum. When admitted she was in a semistuporous condition, with a temperature of 97°; pulse, 110; respirations, 30. Her father and one brother died of consumption, her mother died of "general debility," and one brother became insane. She had the diseases of childhood, rheumatism in her wrists and knees upon several occasions, and "typhoid pneumonia" in 1876. She married when thirty-six years of age, but never became pregnant. Previous to her present illness she used alcohol in moderation, but since then has been taking a couple of "drinks" daily, to relieve her pain. She never was addicted to the use of any drug. For the past ten or twelve years she had been complaining of pain in her stomach at times, and since March, 1907, of severe pain and vomiting. On several occasions she vomited blood and passed blood from the bowels. For some time she has been very tender in the extremities, and for the past few weeks has been confused or delirious.

On examination she was a very corpulent elderly woman, with gray hair and no paralyses. The movements of the eyes could not be tested on account of the patient's condition, but they appeared normal, the pupils being equal, semicontracted, and reacting to light. The tongue was heavily coated, and without tremor. The pulse was rapid, irregular, intermittent, of small volume and low tension. The chest was well formed, the excursion good; the breasts were pendulous. The abdomen was markedly adipose; the skin of the abdomen and chest was smooth and elastic, while that over the legs was rough and dry. Marked tenderness was present all over the body, which did not seem to be limited to the course of the large nerves. Picking up some of the skin caused an outcry of pain, and touching any part of the body (except the face) caused an outcry of pain also. The outlines of the heart were increased downward and to the left and the right; no thrills were detected.

There was a systolic murmur at the aortic area, transmitted into the neck, with accentuation of the second pulmonic and aortic sounds. The breath sounds and pulmonary resonance were normal. The liver dulness extended from the fifth to the eighth interspaces in the mid-clavicular line; the spleen was not palpable but was slightly enlarged to percussion. There were two large bed sores, one on each buttock; another on the outer side of the left thigh. The biceps, triceps, knee, and Achilles reflexes were all absent. The styloid processes of the ulnæ were unusually prominent, a distinct sense of grating being felt in each wrist-joint, more especially in the right.

On November 13, 1907, a bulla about one and one-half inches long and one-half inch wide was present on the internal aspect of the left leg at the junction of the lower and middle third.

On November 14 two more bullæ were present, circular in shape, and about one inch in diameter, one being over the left knee and the other on the inner surface of the leg below the right knee. The urine was alkaline in reaction; had a specific gravity of 1020; contained no albumin and no casts, but did contain many triple phosphate crystals, many epithelial cells, and numerous leukocytes.

On November 17 three more bullæ were observed, a large one on the right heel and a small one at the junction of the metacarpophalangeal joint of each great toe.

On November 18 both albumin and casts were present in the urine.

The stupor gradually deepened, the heart weakened, the lungs became œdematous, and death occurred on November 21, 1907.

Autopsy. The findings were as follows: Fatty infiltration and degeneration of the heart; bilateral emphysema, with atelectasis of the lower lobe of the right lung; chronic diffuse nephritis; slight fatty infiltration of the liver. The subcutaneous fat in the region of the umbilicus was 6.5 cm. in thickness.

Specimens removed for examination were the brain and spinal cord, hypophysis, thyroid gland, adrenal glands, ovaries, and a portion of the subcutaneous fat containing small vessels and nerves.

Sections from the brain and cord were examined microscopically by the usual methods, but did not show any particular changes.

The thyroid gland was normal in size, but presented a marked difference between the lobes—the right lobe being distinctly harder than the left. Microscopically the right lobe showed a marked increase of the connective tissue at the expense of the parenchyma. Many of the acini were very small, the rest being about normal. In the left lobe, the acini were increased in size, many being enormously enlarged. Papillomatous ingrowths or plications, such as were found in a case reported by Dercum, were not observed. In both lobes, but especially in the right, were many areas of round-cell infiltration, not infrequently filling several adjacent acini. A

few small hemorrhagic areas were also observed. The hypophysis was normal macroscopically, but under the microscope, sections stained with hematoxylin and eosin, and hematoxylin and Van Giesen's stain showed areas of round-cell infiltration in the glandular portion. Many cells were degenerated and without nuclei. In the nervous tissue of the posterior lobe were found glandular cells of the same character as those of the anterior lobe, irregularly arranged without any enveloping connective tissue, and being completely surrounded by the neuroglia. This singular condition has been described by Berckley, who claims to have found it in normal hypophyses. I have not seen this arrangement, however, in the sections obtained from any normal pituitaries that I have been able to examine. The adrenal glands presented no abnormalities, except certain irregularities in staining. The ovaries presented marked sclerosis. The fat showed the normal histological appearance, but the nerve filaments presented both interstitial and parenchymatous inflammatory changes.

Case II.—M. W., a female, white, aged forty-eight years, a nurse, was admitted to the medical wards of the Philadelphia General Hospital, September 30, 1903, under the care of Dr. Salinger. On admission she complained of pain in the right foot so severe that she was disabled and could not stand; the right foot was swollen. There was severe pain in the occipital region extending over to the forehead. There was photophobia in both eyes and lacrymation, especially in the right. On the second day of admission she had a severe attack of herpes labialis.

Her maternal grandfather died at the age of eighty-six years, of old age. He was a small sized man. The grandmother died at eighty-four, following a dislocation of the hip. She was a fairly tall woman and very fat, the fat being equally distributed. The patient had five uncles on her mother's side, all of whom were tall and very stout, and three maternal aunts, one of whom was a very stout woman, dying at the age of forty-seven. During the last ten years of her life the latter complained greatly of pains in her legs, which were relieved by massage. Another aunt died at fifty years of cancer of the breast; she was tall and slender. The third aunt is living, is an undersized woman, not stout, and about sixty years of age. The mother of the patient was five feet, four inches tall, very thin and always complained of rheumatism and neuralgia, and died at forty-two from paralysis. The patient states that all of her cousins on her mother's side are large and stout people, but knows little more of them than this. Her father, who is the only known member on the paternal side, was a healthy man up to five years before his death; he died at seventy-six. His right leg was larger than the left, and was very painful. The patient's mother married at twenty-three, had six children, and one miscarriage. Two of the patient's brothers died of accidents. Another died

from typhopneumonia at twenty-two, and a sister died of scarlet fever. The remaining brother is living, is very large, and suffers from rheumatism.

The patient has always been large. She had scarlet fever and chickenpox in childhood. She began to menstruate at fourteen; has always been regular. She had grippe in 1888, and made a slow recovery. She has had three children, and no miscarriages. She states that she had a goitre some twenty-two years ago. She denies veneral disease. She drinks beer, but not to excess.

On October 17, 1903, it was noticed that the patient had a swelling of the right foot that was very painful; it was relieved by massage and bandaging.

On November 3 the right foot again became much swollen and very painful, and at the same time swelling of the thyroid gland, difficulty of deglutition, and pain at the back of the neck were noticed. Subsequently the patient improved, and on December 15, being in good condition and comfortable, she was discharged.

She was readmitted on March 7, 1905, under the care of Dr. Hughes. At this time the diagnosis of myocarditis and nephritis was made, together with adiposis dolorosa. She was seen several times by Dr. Dercum, who confirmed the diagnosis of adiposis dolorosa. She was an extremely large woman, weighing 308 pounds. The superficial fat on the legs was sensitive to palpation. Her general condition was very bad, the pulse rapid, weak, irregular, and of high tension. The respirations were shallow; the expansion was poor. The superficial veins were enlarged. The abdomen was soft and not tender on palpation. The breath sounds were roughened, the expiration prolonged, and a few sonorous rales were audible. The pulmonic second sound of the heart was accentuated. There was a presystolic murmur at the pulmonic area, and the heart's action was irregular. Subsequently the patient suffered markedly from attacks of dyspnœa. Not infrequently she became markedly cyanotic. Gradually she became weaker, and died April 5, 1905.

Autopsy. The autopsy revealed, among other features, marked cardiac hypertrophy with fatty degeneration and chronic nephritis, chronic adhesive pleurisy, œdema and hypostatic congestion of the lungs, and fatty infiltration and congestion of the liver.

The thyroid gland, pituitary body, portions of the fat and skin, and a portion of a radial nerve were removed for examination. The thyroid gland was decidedly larger than normal, particularly the right lobe; the middle lobe was distinctly indurated; the lateral lobes appeared to be normal in consistence. Sections of the right lobe revealed considerable enlargement and dilatation of many of the acini. They were for the most part filled with colloid material. The cubical epithelial lining appeared to be normal, though here and there a tendency to plication of the surface was noted, and in

some of the larger acini, small intrusions and plications into the interior of the acini. In certain portions of the sections decided increase of connective tissue was noted. In these areas the acini were relatively small. No changes were noted in the walls of the vessels. Sections of the left lobe revealed an enormous number of greatly dilated acini. Plications of the cubical epithelium were also noted, occurring somewhat more frequently in this lobe than in the right. Sections of the middle lobe revealed changes similar to those already noted, except that there was a relatively larger increase of connective tissue and a smaller number relatively of large acini. In shape and size the pituitary body appeared to be normal. The capsule seemed normal. This appeared also to be the case with the blood-vessels. The glandular portion presented a couple of small areas of round-cell infiltration, but was otherwise normal. In the nervous portion the same peculiar invasion of the glandular cells was found as in Case I. The fatty tissue revealed no striking changes except here and there some apparent increase in the connective tissue trabeculæ. Separate lipomas were not found. Sections of the radial nerve showed no distinct changes. However, here and there some thickening of the endoneurium existed. The perineurium appeared to be normal. Distinct inflammatory changes were not present.

The recognition of adiposis dolorosa as a clinical entity may be said to date from a paper published by Dercum[1] in 1892, under the following title: "Three Cases of a Hitherto Unclassified Affection, Resembling in its Grosser Aspects Obesity, but Associated with Special Nervous Symptoms—Adiposis Dolorosa." This was prefaced by the report of a single case by the same observer in 1888, as "A Subcutaneous Connective Tissue Dystrophy of the Arms and Back, Associated with Symptoms Resembling Myxœdema,"[2] and another by Henry in 1891.[3] Since the appearance of these papers, about fifty cases of Dercum's disease have been reported, many in detail and quite a number briefly and incompletely. In at least two of the reported cases (Fuchs[4] and Cheevers[5]), the diagnosis is questionable, as the patients had neither spontaneous pain nor pain upon manipulation of the adipose deposits.

Etiology. It has been claimed that adiposis dolorosa may occur in families, but of the two instances reported in support of this statement (Hammond[6] and Cheevers) that of Cheevers may, I think, be ruled out. A family tendency toward obesity, however, is not infrequent. A neuropathic heredity, or a previous personal neuropathic history, has been sometimes noted, but not with suffi-

[1] Amer. Jour. Med. Sci., 1892, civ, 521.
[2] Univ. Med. Mag., December, 1888.
[3] Jour. Nerv. and Ment. Dis., March, 1891.
[4] Wien. klin Woch., 1905, xviii, 706.
[5] Brit. Med. Jour., 1904, vol. i.
[6] Ibid., vol. ii.

cient frequency to make it of any special etiological significance. The disease may occur in either sex, females being affected more frequently than males, in the proportion of six to one. The majority of the cases occur between the ages of thirty-five and fifty years, although cases have been reported as commencing at twelve, seventeen, and nineteen years, and one as late as seventy-eight years. Middle aged women who have passed the menopause form the bulk of the cases.

Alcoholism and syphilis have not infrequently formed a background in adiposis dolorosa, and I differ from those who disregard them as possible etiological factors. The toxic and destructive effects of alcohol and syphilis are well known, and the fact that they frequently cause degenerative changes in the ductless glands was emphasized by Lorand.[7]

It is of interest in this connection to recall the case reported by E. W. Taylor, in which the patient developed adiposis dolorosa while convalescing from acute alcoholic neuritis.

Symptoms. Adiposis dolorosa develops gradually in the majority of cases; a few have a more rapid onset; none has developed abruptly. The cardinal symptoms are: (1) Fatty deposit, (2) pain, (3) general asthenia, and (4) psychic phenomena.

Vitaut[8] has divided the cases of adiposis dolorosa into three groups, depending upon the arrangement of the adipose deposit—nodular, circumscribed diffuse, and generalized diffuse. Of the three, the circumscribed diffuse forms the bulk of the cases, generalized diffuse coming next in frequency. Mixed types, or combinations of these forms, are sometimes seen. While the majority of the subjects are extremely obese, many weighing over two hundred pounds and one reported as weighing three hundred pounds, it should be remembered that in some instances the weight is very little, if any, above the average. This I have seen in two cases of the nodular form. The deposits of fat are found most commonly over the trunk, shoulders, arms, and thighs; the forearms and legs being less frequently affected, and the hands and face but rarely.

Pain and tenderness upon manipulation of the adipose deposits are constant symptoms; this is not true, however, of spontaneous pain, which, while the rule, may be entirely absent. Pain upon pressure over the larger nerve trunks is rare, but has been observed in two reported cases. Diminished sensation is, in my experience, a more common symptom than complete anesthesia, while paresthesias are more frequent than either, being present in some form in almost every case. These paresthesias are sensations of numbness, coldness, burning, tingling, or crawling, variously distributed, and often causing the patients much distress.

[7] An address at a meeting of the Philadelphia County Medical Society, April 12, 1907
[8] Maladie de Dercum, Lyons, 1901.

The asthenia varies in degree from a tendency to fatigue readily, to extreme weakness or prostration. It is distinctly more pronounced than the fatigue of the average neurasthenic, and is a very constant symptom.

The psychic changes that have been observed in adiposis dolorosa have a wide range, with irritability at one extreme and dementia at the other. When we consider the toxic nature of the disease, it is not surprising that confusion and stupor have each been observed. Mental depression, mental hebetude, melancholia, impairment and loss of memory, have also been noted; one patient was an imbecile, three had "epileptic seizures," two had "convulsions," one became "delusional." The most common mental syndrome is that of irritability associated with depression, some failure of memory, and a marked hypochondriacal tendency.

The tendon reflexes may be normal or increased, but are usually diminished or abolished. One case with loss of the skin reflexes has been recorded by Delecq.

Vasomotor phenomena are next in importance to the so-called cardinal symptoms. Under this heading belong the anidrosis, irregular flushings, cyanosis of the extremities, transitory œdema, and the spontaneous hemorrhages from the nose, stomach, and uterus.

Among trophic changes observed in adiposis dolorosa are ulcerations, the formation of blebs and bullæ, arthritic and bony changes. Other symptoms occasionally found are headache, dyspnœa, tachycardia, insomnia, jaundice, and tremor. Blindness was reported in two cases, circinate retinitis in one case, and hyperemia of the disk in one. Deafness was observed in two cases. The blood changes and urinary findings have both been insignificant.

Organic changes in the central nervous system may be looked upon as coincident rather than being actual symptoms. Hemiplegia and aphasia were present in one case, degeneration of the posterior column of the cord in one case, and signs of lateral tract involvement were marked in an unreported case shown by Dr. Dercum in one of his clinics during the last year at the Jefferson Hospital.

A peculiar tendency of the flesh in this disease is that of bruising upon what would ordinarily be an inadequate cause.

Pathology. Of the six autopsies reported to date, together with the two herein recorded, the findings may be briefly stated as follows:

Cases I and II.—Dercum: Macroscopic disease of the thyroid, the glands being enlarged and the seat of calcareous infiltration.

Case III.—Dercum:[9] Irregular atrophy of the thyroid, extensive interstitial neuritis of peripheral nerves in fatty deposits, degeneration in the columns of Goll.

[9] Jour. Nerv. and Ment. Dis., August, 1900.

CASE IV.—Burr:[10] Glioma of the pituitary body; colloid degeneration with atrophy and absence of secreting cells in many acini of the thyroid gland; interstitial neuritis of terminal filaments; sclerotic ovaries.

CASE V.—Dercum and McCarthy:[11] Adeno-carcinoma of pituitary body, thyroid normal, right suprarenal gland hypertrophied, hemolymph glands, interstitial neuritis, undeveloped testicles.

CASE VI.—Guillain and Alquier:[12] Hypophysis doubled in size with marked increase of connective tissue in the glandular portion and changes suggesting an alveolar carcinoma. Thyroid hypertrophied, with increase in connective tissue stroma.

CASE VII.—Price: Inflammatory changes in thyroid, with marked increase in the interstitial connective tissue, one whole lobe being especially infiltrated, the other showing compensatory hypertrophy. Inflammatory changes in hypophysis, with presence of a condition suggesting alveolar or glandular carcinoma, interstitial and parenchymatous neuritis, sclerotic ovaries.

CASE VIII.—Price: Marked increase in the connective tissue of the thyroid gland, dilation of the acini, with infoldings of the cuboidal epithelial lining. The same changes in the hypophysis as were found in Cases VI and VII, but less marked. No abnormalities of the adipose tissue.

Delecq[13] mentions, as causes of adiposis dolorosa, disease of thyroid, testicle, ovary, and pituitary. Raymond[14] says that the cause is not known and the pathology vague. Von Schroeter looks upon the condition as a "dysthyroidismus." Pineles considers that numerous blood glands are at fault, one of the causes being a hypothyroidismus. Frankenheimer[15] believes adiposis dolorosa to be a dystrophy, and compares it to acromegaly, the former affecting the adipose, and the latter the osseous structures.

While the adipose tissue is affected primarily, changes in other tissue have appeared with sufficient frequency to make the occurrence more than a mere coincidence. Cases with joint involvement have been reported by Dercum,[16] Renon and Heitz, and myself.[17] I have also seen one other case with arthritic changes in the knees and small joints of the hands, producing distinct deformity. A case from the Jefferson Hospital showing imperfectly developed bony structures will soon be placed upon record. There may be, therefore, in adiposis dolorosa, arthritic and osseous as well as

[10] Jour. Nerv. and Ment. Dis., 1900, xxvii, 519.
[11] AMER. JOUR. MED. SCI., 1902, p. 994.
[12] Arch. de med. exper. et d'anat. pathol., No. 5, September, 1906.
[13] Presse méd., Paris, 1904, ii, 594 to 596.
[14] Revue neurol. de Paris, 1904, xii, 630 to 632.
[15] Jour. Amer. Med. Assoc., vol. l, No. 13, p. 1012.
[16] Phila. Med. Jour., 1902, x, 1007.
[17] Amer. Med., New Series, vol. ii, No. 5, p. 317.

adipose changes. Muscular atrophy has been observed in one case only, in association with neuritis of the large nerve trunks.

The thyroid, affected in seven of the eight cases, at once commands our attention. Considered from the standpoint of the symptoms however, there is a peculiar contradiction. The obesity, anidrosis, and improvement following the administration of thyroid extract suggest hypothyroidation, while the flushing, tachycardia, tremor, and often the anxious mental state suggest hyperthyroidation. The term dysthyroidismus would seem, therefore, a better one than hypothyroidismus, as used by Pineles.

We should not, however, in considering the pathogenesis of adiposis dolorosa, neglect the hypophysis. It was found distinctly affected in five of the eight cases, and had been unexamined microscopically in at least two of the remaining three cases. In one instance the thyroid was found to be perfectly normal. Vassale,[18] Ponfick, Kr. Gron,[19] Boyce and Beadles,[20] Langhas, Nufice, Dolego, Bourneville, and others have recorded cases with enlargement of the pituitary in myxœdema. Lediard,[21] Lannois, and Pierre Roy have reported cases of acromegaly with marked hypertrophy of the thyroid.

It has also been found that in animals, when the thyroid is extirpated, the pituitary enlarges. Hutchinson[22] regards the pituitary as a growth centre, which belief is opposed by Guerrini[23] who believes that the secretion of the hypophysis is antitoxic in character, and exerts no trophic influence. Guerrini[24] has proved experimentally that the hypophysis reacts to intoxications, either acute or chronic. Madelung[25] reports a case of injury to the hypophysis followed by enormous obesity, while Berger[26] cites an instance of a tumor behind the chiasm, compressing and flattening an otherwise normal pituitary, with increased obesity, alopecia, and dryness of the skin. Magnus-Levy has found an increased oxidation in acromegaly, resembling that which is present in exophthalmic goitre. Malcolm[27] believes that the "nervous" lobe has a katabolic influence on bony tissue.

It seems, therefore, that sufficient attention has not been given the hypophysis, and I would suggest that etiologically it is of almost as much importance as the thyroid gland. May not the symptom group of adiposis dolorosa result from a primary disease

[18] Rivista speriment. di Freniatria e med. leg. d. alien. ment., 1902, xxxviii, fasc. 2, 3, p. 25 to 39; Revue Neurologique, June 15, 1903, p. 560.
[19] Norsk Magazine for Laegendenskabess, August, 1894.
[20] Jour. Path. and Bact., i, 233.
[21] Brit. Med. Jour., April 4, 1903, p. 789.
[22] New York Med. Jour., March 12 and April 2, 1898, and July 21 and 28, 1900.
[23] Centralbl. f. allg. Path. u. path. Anat., March 15, 1905, p. 177.
[24] Archivio di fisiologia, an II, fac. III, p. 384 to 386, March, 1905.
[25] Beiträge f. klin. Chirurgie, 1903.
[26] Ztschr. f. klin Med., vol. lxiv, Nos. 5 and 6.
[27] Jour. Physiol., 1904, xxx, 270.

of either of those structures, the other being involved secondarily through their close interrelation?

Changes in other structures have been mentioned, especially of the genital organs. Undeveloped testicles have been found in one case and sclerotic ovaries in three cases. Symptoms pointing in this direction are the sterility, loss of sexual power, and hypertrichosis in a female. These changes, however, together with the neuritis of the terminal filaments, appear to be secondary in importance to those in the thyroid and hypophysis.

Diagnosis. A typical case of Dercum's disease should be easy of recognition. The diagnosis should be based chiefly upon the two symptoms—accumulations of adipose tissue, and the presence of pain upon manipulation of these deposits. From multiple neuritis, the diagnosis can be made by the absence of pain and tenderness over the larger nerve trunks, or, when this is present, by the absence of muscular wasting commensurate with the duration and intensity of the pain. In simple lipomatosis there is no pain, and the general symptoms of adiposis dolorosa are absent. In its early stages, the disease has not infrequently been mistaken for rheumatism.

Prognosis. Recovery from adiposis dolorosa is rare, but the disease itself does not directly cause death. Its tendency is usually progressive—often with exacerbations of pain accompanied by increase in size of the adipose deposits. Complete intermissions are rare, but remissions are common.

Treatment. The present status of the treatment of adiposis dolorosa leaves much to be desired. At best it is uncertain and unsatisfactory, but by no means hopeless. As in other forms of neuritis, the salicylates are often of value in relieving the pain, and may be advantageously combined with a bromide salt, as the latter tends to lessen the disagreeable effects of the former. Aspirin, being less irritating to the stomach than the ordinary preparations, is often of value. Extract of the thyroid gland, while not a specific, is the most valuable remedy at our command. Several cases have been reported as showing marked improvement following its administration, and Dercum cites one case of cure (the only cure reported) following its use. In my own experience, I have seen five cases distinctly benefited by its administration. It is obvious, however, that the brilliant results obtained in myxœdema, cannot here be expected. The therapy of the pituitary body is at present so indefinite and so little understood, as to make administration of the gland of no practical value.

Potassium iodide should be given whenever there is present a definite history of syphilis, but I have never seen any beneficial results following its administration, even in a case having a specific history.

As the majority of the patients are obese, the heart is likely to be

involved in the general adiposity, and may require attention. More general measures, as massage, electricity, rest, etc., frequently add to the comfort of the patient and should never be neglected.

I regret to say, however, that in some cases, fortunately a minority, the symptoms are unrelieved by any of the various remedial measures that have been recommended. As the years bring us a more accurate knowledge of the normal and pathological chemistry of the secretions of the ductless glands, we may hope for more definite therapeutics, and better results in the treatment of this interesting disease.

I desire to express my indebtedness to Dr. F. X. Dercum for the privilege of reporting the cases, and to Dr. W. M. L. Coplin, for many valuable suggestions.

THE CHEMISTRY OF THE URINE IN DIABETES MELLITUS.

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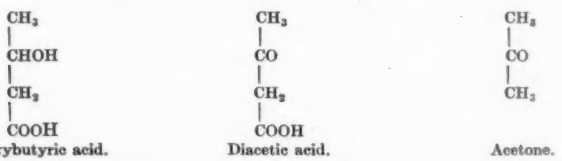
The history of the case which formed the basis of this study is briefly as follows: M. H., a female, aged seventeen years, was admitted to the Montreal General Hospital, in Dr. Finley's service, on January 6, 1908. The family history was negative for diabetes. The personal history was negative until July 28, 1903, when she had an "interval operation" for appendicitis. The urine during this admission had a specific gravity of 1015 and was negative for both albumin and sugar. She was discharged August 19, 1903, the wound having healed "per primam." Two weeks later she developed typhoid fever, during which the wound broke down. On February 16, 1904, she reëntered the hospital to have the sinus closed. The urine was again negative for albumin and sugar and had a specific gravity of 1022. In March, 1906, the appendix wound a second time broke down, and after a prolonged home treatment she was re-admitted on October 6, 1906; the sinus was excised and the edges freshened. The wound closed very slowly, and on her discharge, on November 17, 1906, had not completely healed. The urine was examined three times during October, 1906, but contained no sugar, though the specific gravity was high (1032, 1030, and 1023). The patient felt perfectly well until June, 1907, when she first suffered from weakness, polyuria, and thirst; these symptoms gradually increased in intensity. During November and December, 1907, she noticed an increase in appetite and a tendency to attacks of som-

nolence which lasted for a day or two at a time. She had lost thirty-one pounds in weight in seven months.

Physical examination revealed a fairly well developed but poorly nourished girl; mucous membrane pale; expression dull and listless, but mind clear. Skin dry and harsh, but no evidence of pruritus. The lymphatic and respiratory systems were normal. The circulatory system was negative except for a somewhat "clicking" aortic second sound and slight thickening of the radials. The tongue was clean and moist; the teeth carious. The breath had a sweet fruity odor. The abdomen was negative except for some tenderness in the right hypochondrium. The eye grounds were negative. The temperature ranged between 99° and 99.2°; pulse, 70 to 96; weight, 98½ pounds.

She was placed on the ordinary ward diet from January 7 to 20. The amount of urine varied between 6050 and 3730 c.c., with an average of 4680 c.c. in the twenty-four hours. The fluid intake was 2640 to 4120 c.c. or an average of 3160 c.c. in the twenty-four hours. The reaction of the urine was strongly acid. The specific gravity was 1035 to 1044, the average, 1031.5. There were evidences of a slight grade of nephritis, as shown by a constant albuminuria and occasional hyaline and granular casts. The sugar content, both by the saccharometer and by Fehling's titration method, was very large. The percentage by the former varied from 6.38 to 9.46 per cent., and by the latter 7.24 to 9.8 per cent.; the amount in twenty-four hours by Fehling's method averaged 370.6 grams, with a maximum of 495.5 grams and a minimum of 278.3 grams. This is, of course, a large amount of sugar, and shows a considerable derangement of the carbohydrate metabolism.

The Acetone Bodies. It must be borne in mind that normally acetone occurs in the urine in small but detectable amounts (0.01 to 0.05 gram in twenty-four hours). Acetone is an oxidation product of diacetic acid, and this in turn of β-oxybutyric acid. A glance at their structural formulæ will be useful.



β-oxybutyric acid. Diacetic acid. Acetone.

It is now generally conceded that the acetone bodies originate chiefly from the lower fatty acids of the organism and of the food. They may arise from proteid (leucin) to a very slight extent. Their excretion in the urine (known as ketonuria) occurs in the absence of normal carbohydrate metabolism; neither the largest intake of fats nor the greatest increase of fat destruction in the body will lead to a ketonuria, as long as sufficient carbohydrates are breaking down.

The daily combustion of 80 to 100 grams of carbohydrates is sufficient to prevent it. The carbodydrates provide the oxygen necessary for complete oxidation of fat into CO_2 and H_2O; deficiency of carbohydrates causes a defective oxidation in the tissues, hence defective fat metabolism with resulting acetone formation. Normally there is excreted 0.01 to 0.05 gram of acetone, but if carbohydrates be withdrawn the acetone increases twenty to fifty times and both β-oxybutyric acid and diacetic acid may appear in the urine. When the ability of the organism to attack the circulating carbohydrates has received a severe injury, when all carbohydrates of the food re-appear in the urine, when the greatest portion of the sugar arising from the albumin is excreted, then the typical ketonuria occurs. Ketonuria is a useful measure of the intensity of the diabetes; thus, in the first stage of diabetes acetone only occurs; in the second stage both acetone and diacetic acid, and in the third stage all three bodies appear. Further, much acetone is excreted by the lungs, giving the characteristic fruity odor to the breath.

Estimation of Acetone and Diacetic Acids. The usual method is that of Messinger-Huppert, based upon Lieben's observation that acetone when treated with iodine in solution gives rise to the formation of iodoform. This method determines both acetone and diacetic acid, as the latter is decomposed by 100° C. into acetone and CO_2. Our patient showed a great excess of both these bodies, varying from 3.8793 to 1.2143 grams, or an average of 2.907 grams in twenty-four hours. Von Noorden states they seldom exceed 5 to 6 grams, though rarely 7 to 8 grams have been observed. Gerhardt's ferric chloride test for diacetic acid was positive on the first two days only.

Estimation of the β-oxybutyric Acid. This was carried out as recommended by Pavy. This acid is levorotatory, while glucose is dextrorotatory, therefore one counteracts the other, causing a considerable discrepancy between the sugar as determined by the saccharometer and that by Fehling's titration. The latter gives the true amount of glucose, while the former gives the excess of glucose over the levorotatory oxybutyric acid. The difference between the two readings gives the amount of the acid in terms of glucose. To express it in terms of oxybutyric acid (which has an optical activity of 24.1° as against that of glucose of 52.5°) one multiplies the difference by 2.2. This method is open to error from the presence of other levorotatory bodies, as levulose, and is not as exact as the direct chemical methods of Darmstaedter and others. Nevertheless, it was found that the acid varied in amount from 98.96 to 33.76, with an average of 61.424 grams. It is not uncommon to find 60 to 70 grams of this acid in the twenty-four hours; it may even exceed the sugar in amount.

Nitrogenous Bodies. The total nitrogen of the urine was estimated by the Kjeldahl method and was found above the upper limits of normal (10 to 16 grams), ranging from 14.4155 to 18.4703, or an average

of 16.8232 grams. This increase is physiological in diabetes, and is due to the great increase of proteid ingestion, which is often more than 180 to 200 instead of the normal 90 to 100 grams. It becomes pathological, when, in addition, the body albumin is excreted, which occurs with a high sugar output. The nitrogen loss is greater the more the general nutrition is injured by the glycosuria; it is small when the food contains enough albumin and much fat. The toxic bodies of coma cause much nitrogen loss.

The urea is increased for the same reason as the total nitrogen, and was found to range between 37.3 to 61.65 grams, with an average of 42.93, as compared with the normal limits of 20 to 40 grams.

The uric acid is normal or slightly increased. Our patient excreted 0.1979 to 0.6714, or an average of 0.3783 gram, while normally it varies from 0.2 to 1.5 grams. The extractives, kreatinin, etc., were not estimated.

Ammonia. The NH_3 content is most important and was estimated by Schaffer's modification of Schlösing's method. This is by no means an ideal method, and has a considerable error when compared with Folin's precedure. Normally the urine contains 0.5 to 0.1 gram, but may reach 1.2 to 1.5 grams on a meat diet. Our patient showed 4.8698 to 3.8847 grams, with an average of 4.251 grams during the first four days. In diabetes 3 to 6 grams is common, and there is a case in literature which excreted 12 grams in the twenty-four hours. The high values of NH_3 occur in the severest cases and especially in diabetic coma. It is an attempt on the part of nature to protect the "native alkalinity" of the tissues from the acidosis present. It will be remembered that the sulphur and phosphorus of the proteids are oxydized into H_2SO_4 and P_2O_5. Normally these acids encounter sufficient fixed bases to neutralize them, but when they are in excess they have to attach themselves to a portion of the NH_3, which is at the same time produced by proteid destruction, and in this state pass into the urine. Normally the NH_3 in the urine is small, for it combines with the CO_2 to form urea, but when NH_3 is combined with sulphur or phosphorus it cannot also combine with CO_2. Further, when diacetic and oxybutyric acids are present they carry off still more NH_3. Another point of interest is that the relation of the nitrogen of the NH_3 to the total nitrogen is much increased in diabetes and often forms 10 to 20 per cent., instead of the normal 2 to 5 per cent. In our case the NH_3 nitrogen formed 20.8 per cent. of the total nitrogen. In conclusion, the ammonia determination gives an accurate estimation of the acidosis present and one more easily arrived at than the direct estimation of the acidosis itself.

Treatment. The only treatment during the first two weeks was the administration of a pill of opium, one-half grain, three times a day. On January 21 the patient was placed on a strict von Noorden diet plus 120 grams of bread; after two days the bread was reduced to 100 grams. This dietary was given to January 25, when it was discon-

tinued on account of weakness and drowiness being complained of by the patient.

The Urinary Findings. The quantity fell to 2015 c.c. on the third day and remained about that point for three days, though the fluid intake was but little restricted, being about 2300 c.c. The amount of sugar fell on the third day to 20.15 grams, but rose again to 92.39 on the fourth day. The acetone fell to 2.0189 grams on the fourth day, when the diacetic acid re-appeared. On the fifth day the acetone had risen to 4.06 grams and the diacetic acid was still present. β-oxybutyric acid, which had fallen to 34.5774 grams on the third day, rose to 54.67 grams on the fifth day. The NH_3 showed little change on the third day, being 3.6858 grams, but on the fifth day it rose to 4.195—the highest point observed since the second day after admission.

As diabetic coma was threatening, as shown by the patient's general condition (weakness and somnolence) and the urinary findings, the strict diet was discontinued, with an immediate improvement in the symptoms, the disappearance of the diacetic acid, and a drop in the β-oxybutyric acid and ammonia, though the acetone rose still more, to 4.69 grams. Now the object of a carbohydrate-free diet is to restore the metabolic equilibrium of the patient's organism, which has been upset by the toxic effect of the abnormal presence of sugar in the system; by the removal of this influence metabolism may return to its orderly mode of procedure. It must also be remembered that upon withdrawal of carbohydrates, even in health, a small amount of the acetone bodies appears in the urine, which after a time gradually disappears. Hence there is a constant and real danger in the treatment of severe cases of diabetes from the too sudden withdrawal of carbohydrates. Last year I saw a patient who died in coma developing on the fifth day after the institution of a strict carbohydrate-free dietary. Upon the day of his death the urine contained 255.36 grams of sugar, 3.9639 grams of acetone, and 67.54 grams of oxybutyric acid. I cannot state positively that the onset of coma was due to the strict diet, for the case was a very severe and very acute one, but from the experience of others there is a very strong presumption that the onset of coma was at least hastened. Unfortunately for my contention, I had no opportunity to make the necessary determinations before the onset of coma.

It cannot be too often and too strongly emphasized that in severe cases the withdrawal of carbodydrates must be done cautiously and a simultaneous careful examination of the urine made. Hence a patient should be in a hospital with a clinical chemist in the laboratory, or the physician should himself be in a position carefully to watch the urine for signs of ketonuria, which may be present for days before coma supervenes. The various points to be emphasized in carrying out a von Noorden diet can be best illustrated by the following account: After the warning received, the patient was left on a

full diet and was given large doses of sodium bicarbonate until April 1, when a strict diet plus 100 grams of potatoes plus 150 grams of bread was given. This represented in units of energy 2000 calories. Now, for a healthy girl of her weight, 100 pounds, or 45.4 kilograms, there is required for proper nourishment when at rest (45.4 x 35) 1600 calories; hence she was getting an apparent excess of her needs of 400 calories. But she was excreting 269.9 grams of sugar, that is, a daily loss of 1100 calories. The diet then had for her the value of 2000 — 1100, or 900 colories. Since the nutritional demands were 1600, there was an actual deficit of 700 calories. In other words, the body was consuming for the necessary supply of heat and energy a daily value of 700 calories. The substance consumed was body fat, as shown by the loss of two pounds in weight. This was not ideal, and, therefore, the proteids were almost doubled, with the result that she held her weight for the next three days. One must always be careful that the caloric value of the food is sufficient to meet the needs of the organism, due allowance being made for the loss of energy by the sugar excretion.

Date.	Diet.	Calories.	Body weight pounds.	Fluid intake c.c.	Amount urine c.c.	Specific gravity.
Normal.		1600			1200	1015–1025
Jan. 7–20	Ward.	.....	98¼	3160	4680	1037
Jan. 23	Strict + 100 grams bread.	2600	98½	2240	2015	1018
Jan. 24	Strict + 100 grams bread.	2600	.....	2240	1905	1034
Jan. 25	Strict + 100 grams bread.	2600	96½	2360	3180	1032
Jan. 26	Ward.	.....	.....	2740	5110	1030
March 31	Ward.	.....	98	1000	2970	1033
April 3	Strict + 150 grams bread + 100 grams potatoes.	2000	95	1200	1680	1037
April 14	Strict + 75 grams bread + 100 grams potatoes.	2230	92¼	1300	2990	1037
April 21	Strict + 25 grams bread + 100 grams potatoes.	2750	93½	1300	905	1031
April 28	Strict.	2700	93½	1300	1220	1038
May 1	Strict + 100 grams bread.	3160	94¾	1000	910	1038
June 3	Strict + 100 grams potatoes.	2700	98	2020	1820	1026
June 5	Strict.	2660	99	1700	2160	1038
June 7	Vegetable.	3490	100	1790	1880	1035
June 11	Oatmeal.	2910	105¼	1220	3360	1034
June 14	Strict.	2660	104¾	1080	3610	1035
June 17	Vegetable.	3450	105½	940	2770	1036
June 20	Oatmeal.	2590	105	1040	2215	1028
June 26	Strict + 100 grams bread.	2885	105¾	1000	2260	1031
June 30	Strict + 50 grams bread.	2770	108	1360	3060	1030
July 3	Strict + 60 grams Na_2CO_3.	2770	108	1220	3030	1027
July 5	Strict + 60 grams Na_2CO_3.	2770	113	1340	2460	1031

Date.	Sugar by Fehling.	Sugar by saccharometer.	Acetone plus diacetic.	Diacetic acid.	β-oxybutyric acid.	Total N, grams.	NH_3, grams.	Urea, grams.
Normal.	0	0	0.01–0.05	0	0	10–16	0.5–1	20–40
Jan. 7–20	370.6	342.68	2.907	x	61.424	16.82	4.251	42.93
Jan. 23	20.15	4.43	2.533	0	34.577	19.09	3.685	37.28
Jan. 24	92.39	71.24	2.018	x	46.52	15.22	2.887	34.77
Jan. 25	199.75	174.9	4.065	x	54.67	20.87	4.195	47.7
Jan. 26	304.04	281.05	4.694	0	50.56	19.53	3.023	45.9
March 31	269.97	235.22	1.372	0	76.44	... ...	2.019	... ...
April 5	118.27	92.40	2.430	x	56.91	11.14	2.810	26.88
April 14	142.32	105.24	5.527	xx	81.56	... ...	... ...	... ...
April 21	22.89	16.92	0.894	x	13.14	11.20	2.547	19.91
April 28	21.71	16.10	0.592	xx	12.34	17.48	... ...	34.16
May 1	46.865	42.04	0.220	0	10.61	11.91	1.120	22.95
June 3	26.75	12.01	1.700	xx	32.43	... ...	... ...	... ...
June 5	73.57	57.02	1.240	xx	37.06	... ...	... ...	... ...
June 7	94.94	78.58	1.741	xx	35.41	... ...	... ...	... ...
June 11	220.75	206.97	2.488	0	30.30	9.78	4.889	23.52
June 14	277.60	238.26	3.197	x	86.56	16.07	6.137	36.10
June 17	173.12	158.44	2.507	?	32.29	10.39	3.239	24.93
June 20	119.05	107.20	1.821	0	26.06	9.11	3.690	21.04
June 26	126.78	109.38	2.242	0	38.28	14.55	3.447	33.90
June 30	165.85	134.64	4.912	xx	68.66	18.02	3.641	41.30
July 3	168.16	146.65	2.566	0	47.32	17.13	3.852	... ...
July 5	114.88	92.00	2.236	0	50.33	8.33	3.228	27.3

x = Good reaction. xx = Marked reaction. ? = Doubtful reaction.

The aforementioned diet was maintained for three days; then 25 grams of bread was withdrawn; this was repeated at intervals of three days, until by April 23 the patient was getting no bread and but 100 grams of potatoes. After the usual period of three days the potatoes also were withdrawn. To make up for the loss of calories by this carbohydrate withdrawal the proteids and fats were increased to almost three times the original amounts, so that she was getting from April 22 to May 1 about 2650 calories, that is, an apparent excess of 1000 units, while she was losing on an average (58 x 4.1) 240 units, hence she was getting 760 calories above the requirement of even her disordered metabolism. As a result, she held her weight remarkably well, weighing, thirty-one days after the institution of the diet, 94¾ instead of 97 pounds, that is, a loss of 2¼ pounds. The amount of urine fell gradually from 2800 c.c. on April 1 to 905 c.c. on April 21, again rose slightly to 1300 c.c., to fall once more to 910 c.c. on May 1, that is, to less than one-third of its original volume, though the intake of fluids was only reduced from 1200 to 1000 c.c. in twenty-four hours. As might be expected, the specific gravity of the urine showed little change, varying between 1031 and 1038.

The sugar fell from 269.973 grams on March 31 to 21.716 grams on April 28, the third day of the carbohydrate-free diet. The patient, though showing a markedly diminished sugar excretion, never became "aglycosuric;" she "manufactured bricks out of straw," or, more truthfully, she was manufacturing carbohydrates from her own tissues. Only the severest type of diabetes remains glycosuric under strict dietary, and to such a class does our patient belong. It was not considered advisable to keep her on this strict diet longer than three

days. Accordingly she was given 100 grams of white bread on April 29, and it was found that her carbohydrate tolerance had been considerably increased by this cure, as on May 1 she excreted only 46.865 grams of sugar instead of 199.75 grams excreted under similar conditions on January 25, 1908. This is the usual result of the von Noorden diet and the chief aim of the *regime*. This increase of carbohydrate tolerance lasts for some time, and in mild cases may reach such a degree that no sugar is excreted even after the ingestion of large amounts of carbohydrates (300 grams and more).

The effect on the acetone was also observed: At first it rose from 1.3728 grams on March 31 to 2.4303 on April 3, but fell again to 0.5922 gram on April 28. This is the usual course of events if the carbohydrates be gradually withdrawn, that is, first a rise and then a gradual fall as the organism gradually accustoms itself to the altered conditions. The ferric chloride reaction for diacetic acid reapperaed and was very marked on April 28. The oxybutyric acid persistently fell from 76.44 grams on March 31 to 12.34 grams on April 28. Upon the addition of 100 grams of bread to the strict diet on April 29, the acetone three days later still further fell to 0.2207 gram, and the oxybutyric acid to 10.6106 grams, while there was no reaction for diacetic acid. The ammonia fell from 2.0196 grams on March 31 to 1.9744 grams on April 27.

As the patient grew restless, she was allowed to return to her home on May 7, with directions to carry out the strict dietary plus 100 grams of bread daily for three weeks out of each month. She was readmitted on May 27 on account of a return of her symptoms. On June 3 she was placed on a strict von Noorden diet with a caloric value of 2660 units. On June 5 the urine showed a change for the worse in quantity (2160 c.c.), specific gravity (1038), total sugar (73.8 grams), and β-oxybutyric acid (37.06 grams). The diacetic reaction remained unaltered and the acetone (1.2 grams) was less than on the first day of strict diet by nearly 0.5 gram.

Accordingly, on June 6 the green vegetable diet of von Noorden was tried. This consists of large quantities of green vegetables (150 grams), the yolks of ten eggs, 225 grams of bacon, 100 grams of butter, bouillon, and coffee with cream. Its caloric value was 3490 units, or an excess above her needs of 1500 calories. She gained two pounds in weight, but while the amount of urine, its specific gravity, and the oxybutyric acid fell somewhat, the sugar (91.94 grams) and the acetone (1.74 grams) increased and the diacetic acid persisted. This was contrary to the findings of von Noorden, who believes that this dietary causes a fall in the excretion of sugar and the acetone bodies.

We next tried the oatmeal cure of von Noorden for three days. It consists of 250 grams of oatmeal, 200 grams of butter, 6 eggs, 150 c.c. of coffee or tea with cream, 120 c.c. of lemon juice, and 50 c.c. of brandy. This has a caloric value of 2910 units, or an excess of 400

calories. There was a striking increase in body weight of 5¼ pounds by the third day. The amount of urine was almost doubled (3360 c.c.) and the sugar almost trebled in quantity (220.7 grams). The acetone (2.48 grams) also showed an increase, but the diacetic acid test was negative and the oxybutyric acid showed a slight diminution (30.3 grams). The quantity of ammonia was very large (4.889 grams) and the urea about normal (23.5 grams). As was to be expected, the total nitrogen (9.78 grams) was below normal limits. Here again the urinary findings do not bear out von Noorden's claim that such a dietary is followed by a fall in the excretion of the sugar and acetone bodies. The supposed efficacy of this diet lies in the fact that diabetics bear large amounts of one form of carbohydrates better than small amounts of several carbohydrates. Von Noorden, however, admits that the oatmeal diet is not suitable for all cases; some it benefits and others it actually harms. We then decided to repeat the three dietaries, each for a period of three days. We were very disappointed to find upon the third day of the strict meat diet that the total quantity of urine (3610 c.c.), and sugar (277.6 grams), and acetone (3.19 grams) had still further risen, while the ferric chloride test was again positive and the oxybutyric acid reached its highest point (86.56 grams) at any time during our observations of the case. Corresponding with the acidosis the ammonia was also at its maximum (6.137 grams) in contrast to the total nitrogen (16.07 grams) and urea (36.1 grams). We were at a loss to explain this unsatisfactory result, as no symptoms of coma manifested themselves. It could only be further proof of the severe type of the disease. Our surprise was great, and we felt once more encouraged when on the third day of the second vegetable cure the urine showed the sugar to have fallen to 173 grams, the acetone to 2.5 grams, and but a doubtful ferric chloride test to be present; the oxybutyric acid also fell to 32.298 grams and the ammonia to 3.239 grams. The third day of the second oatmeal cure showed still further improvement in the sugar (119.05 grams), the acetone (1.82 grams), the oxybutric acid (26.063 grams), while the ammonia remained practically unaltered (3.69 grams).

After another three days of strict dietary the patient was given an additional 100 grams of bread to ascertain whether the carbohydrate tolerance had been increased by these "cures," as had been the case, on her former admission, by the strict von Noorden dietary. On the third day (June 26) there was considerable increase in her toleration for carbohydrates, for the sugar amounted to only 126.78 grams as compared with 277.6 grams of June 14 after the first series of diets; but this increase of tolerance was not as striking as that which occurred in April and May in the early stage of the disease; further, it was not maintained, for by June 30, when there was an allowance of but 50 grams of bread, the sugar rose again to 165.8 grams, the

acetone to 4.9 grams, the oxybutyric acid to 68.66 grams, with a strong reaction for diacetic acid.

It was now decided to watch the effect of the administration of sodium bicarbonate upon the ammonia and acidosis. For the purpose 60 grams of the powder was given in four divided doses in the twenty-four hours. The urine was examined on the third day (July 3) and fifth day (July 5), when the patient was receiving a strict meat diet plus 50 grams of bread. Whereas, under the same diet the oxybutyric acid had been, on June 30, 68.66 grams, it was now 47.328 and 50.331 grams, a slight but definite decrease. The ammonia remained practically unaffected, being 3.6 grams before, and 3.8 and 3.2 grams after the administration of the sodium carbonate.

From a study of the chemistry of the urine during the months of June and July it was evident that the disease was making rapid strides and the usual benefits from diet were not accruing. It was decided, therefore, to allow the patient to return to her home, and a still gloomier prognosis was given.

On September 19, 1908, while I was absent from town, she was again admitted to the hospital. The urine was not so elaborately studied as on previous admissions, but contained excessive amounts of sugar, acetone, and diacetic acid. She was placed on ward diet until September 25, when she was given a strict meat diet plus 50 grams of bread. This caused some diminution in the sugar excretion, but both acetone and diacetic acid were present qualitatively. The bread was gradually reduced to 30 grams by September 30. On September 29 the patient began to feel drowsy and to vomit and to complain of abdominal pain. Suddenly on the night of October 1 there was severe epigastric pain, extreme restlessness, air hunger, vomiting—in short, all the symptoms of rapidly developing coma. The urine showed a diminished amount of sugar, but an increase in intensity of the acetone and diacetic qualitative tests. In spite of an attempt to combat the acidosis by intravenous injection of normal saline and sodium carbonate solutions, drowsiness rapidly set in, the fruity odor of the breath became more marked, the pulse failed, and by 7 P.M. of October 2 (that is, four days after the onset of the first symptoms and less than twenty-four hours after the severer manifestations) she became deeply comatose. For three to four hours immediately after the intravenous injection the patient seemed to improve, but she lapsed again into coma and died at 5.30 A.M. of October 4—eighty hours after the onset of coma.

The autopsy performed seven hours after death revealed parenchymatous nephritis, pulmonary tuberculosis, and chronic pleuritis. The pancreas showed no gross or microscopic change. There was a slight but definite fatty degeneration of the heart, kidneys, and liver.

INTESTINAL OBSTRUCTION: AN OUTLINE FOR TREATMENT BASED UPON THE CAUSE OF DEATH.

A STUDY OF FOUR HUNDRED EXPERIMENTALLY PRODUCED LESIONS.[1]

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Physiologists often quote the sentiments of Montaigne: "With how little anxiety do we lose the consciousness of light and of ourselves." By this they would convey the idea that the act of dying is as painless as the act of falling asleep, and also as little perceived. Nevertheless, so strongly rooted in the human mind is the desire to live, that the profession of medicine has for its chief purpose the lengthening of human life. Hence, it is natural that the study of the causes which bring death to a cell, to an individual, or to a race of men has for long been a favorite and engrossing one. None of us without giving thought can realize how many and how different are the actual and underlying causes which terminate life. "The supreme fact," says Adami, "that sooner or later death comes to all men has profoundly affected all human thought, and the various religions of the world may be regarded as the evidence of man's determination to rise superior to the dissolution of his body." In the unicellular organism there is no destruction of the essential living matter but a multiplication thereof: each spore carries on the life. There is no death in the ordinary interpretation of the word. "It is with the appearance of the multicellular organisms that natural death enters into the world." In the cellular differentiation it comes about that the germ cells are given the inherent power of perpetual life, while the somatic cells, through the elaboration of which the individual organism reaches its final development—side-tracked groups, as it were—are destined to hold and live together for a span and then to undergo dissolution.

There are in general two forms of death which may befall the somatic cell—the physiological and the pathological. The pathological form of death may be induced by mechanical, physical, chemical, or bacterial agents. With these in this paper, which deals with the cause of death in duodenojejunal obstruction alone, I hope to demonstrate that we are not concerned. Physiological death, on the other hand, that form of dissolution of somatic entity

[1] A research conducted under a grant from the Rockefeller Institute for Medical Research, and presented at a meeting of the Johns Hopkins Medical Society, Baltimore, March 1, 1909.

which has been studied so thoroughly, so exhaustively, in the pioneer work from the Johns Hopkins laboratories, the death following parathyroidectomy and that associated with adrenal and pituitary destruction or removal, this physiological form of death is that which immediately concerns us. I understand physiological death to comprise not only the dissolution which follows the removal of certain substances by destruction of their secreting cells, such as the parathyroid, but also that dissolution of somatic life which is brought about by the mechanical interference with detoxication of the normal secretions of the body. Putting it concretely, I may say that a barrier which may prevent the normal distribution of enterokinase, or the normal reaction of anti-enzyme upon enzyme, is the cause of death which is physiological and somewhat of the same type as is the death brought about by removal of glandular secretions, so-called internal in character. It is not to be denied, of course, that these thoughts suggest ascribing to the duodenum a function, I believe, hitherto and as yet unknown, that of internal secretion.

In whatever manner this may be rightly considered, I ask you to allow me to start with the hypothesis that the intestinal barrier which closes the lumen works no ill to the organism save through an interference with the physiological exchange or balance of the duodenojejunal secretions, and that the resulting death is physiological in type. I ask you to assume for the moment—and for this we have adequate proof—that in intestinal obstructions there is no appreciable damage to the individual through the nervous system from the direct trauma of the obstruction; that there is no lethal infection of bacterial origin; that the element of decomposition of food does not enter into the picture at all—in short, that all pathological forms of death are eliminated. I shall strive to detail to you the simple, and withal possibly inefficient, measures which I have taken in my efforts to prove these things to myself.

Nervous Effect of Intestinal Trauma. Clinically surgeons have recognized a difference of degree in the shock produced by cutting the intestine in various places: the nearer one approaches the pylorus, other factors being equal, the greater the shock. Indeed, in the execution of the well-known pyloroplastic operation devised by Finney, it has been, I believe, commonly recognized that a shock to the patient might occasionally be clinically noticeable at the moment of actual section of the pylorus. Operations which will be described later and in the course of which this highly sensitive mechanism was entirely removed or seriously injured, and furthermore operations in the remotely aboral portions of the small intestine which technically were associated with precisely the same amount of traumatism as those in the duodenum and jejunum, afford, under study, point blank evidence that the nervous shock or reaction (let it be called what it may) has nothing whatsoever to

do with the cause of death in the form of intestinal obstruction under consideration. Indeed, I have been led to the conviction that the infliction of even unusual mechanical traumas incident to various operative procedures upon the alimentary canal, not excepting the thoracic œsophagus, is incapable of producing more than a transient and unimportant nervous reaction. It stands to reason that if a dog would live for weeks with iliac obstruction and dies at the end of a few hours with duodenal obstruction, and that if the same dog can be made to live also for weeks, if but the slightest drainage be instituted, something far more important than mere mechanical injury is the cause of death. Obviously the traumatism in each case is equal. Incidentally, it may be noted that whatever nervous traumatism might be associated with the dilatation of the proximal loop, would presumably be greater where the greater dilatation occurred. In the majority of fatal cases of duodenal obstruction, there was little or no dilatation; it rarely has time to develop, whereas in the chronic aboral obstructions it is frequently found.

Infection of Bacterial Origin. No one could pretend to read the literature of intestinal obstruction and not be acquainted with the contributions which have been made from the Johns Hopkins Laboratory on the subject of bacterial emigration oral to the obstruction. These studies have contributed widely to our knowledge of the pathological type of death which unquestionably occurs from obstructions in the aboral portions of the ileum and from occlusions of the great gut. It is, however, the physiological form of death alone with which I am concerned; with the fulminating prairie-fire-like toxemias which, unheralded and often in a few hours, destroy the victims of duodenal obstruction. In dogs the clinical syndrome is usually typical; the muscular tremors localized in certain groups of muscles, the tachycardia, the rapidly advancing coma and death, followed by a characteristic stiffness. Clinically this picture is not far different from that observed after parathyroidectomy.

The pathological form of death which results from obstruction at or near the ileo-cecal valve and which may well be of bacterial or stercoraceous origin, has not been the special object of our study, and of it, therefore, I am not qualified to speak. I would note, however, in passing that it is slow and tortoise-like in overtaking the somites, suggesting in every detail a process quite different from that which has been the special subject of my studies. Furthermore, it should be noted that while the duodenum possesses a rich flora, it is exceedingly poor, at least in the healthy dog, in pathogenic forms, and continental observers, as well as your own, have found blood cultures taken from cases of duodenal obstruction entirely sterile.

With these premises then I ask you, for the academic purposes

of argument, to assume that in obstruction of the intestine two entirely separate and distinct forms of death are to be differentiated: the one duodenal and purely physiological, due to an unknown disturbance of the duodenal secretion or balance, the other ileo-colic and purely pathological; the one a true auto-intoxication, the other a true exo-intoxication.

DUODENAL AUTO-INTOXICATION. The following impressions have resulted from the study of over 400 cases of duodenal or oro-jejunal obstruction produced experimentally during the past five years at the Surgical Research Laboratory of Columbia University. Although the series is not small, the positive conclusions which are offered by it are regretfully small. This may be attributed in part to the natural deficiencies of the experimenter and to the great intrinsic difficulty of the task, and also very fairly in part to the fact that the work has been done at odd moments taken from an annoyingly engrossing practice and amid surroundings sadly incomplete and unfit. I mention this because I seek your indulgence.

A chronicle of the steps which have led to the above outlined position on intestinal obstruction is as follows: About five years ago, while modifying the McGraw elastic ligature so as to substitute common every-day twine for the perishable elastic, and also with a view to remove sizable apposed portions of gut and stomach wall, Dr. Weir at the time considering this a necessary part of the technique, we were suddenly confronted by the perplexing coincidence that all our animals died. There was no peritonitis; there was no gross lesion discoverable within or without the abdomen. We noted an early rigor mortis, and that before death the heart beat was accelerated, the gait was peculiar, owing to spasticity of the hind legs, and there were well-defined muscular twitchings. The technique had embraced the closure of the duodenum (Fig. 1). At that time no information was forthcoming as to the cause of these phenomena and I could find nothing regarding it in the literature. It was not long, however, before Roger, in France, began an allied series of experiments which to some extent corroborated our own findings. All these experiments, as well as the most recent ones, have been based on the utilization of this potential gastro-enterostomy by the twine triangular ligature as a control. It seems reasonable, and indeed is easily susceptible of proof, that the twine will cut out and give drainage in healthy stomachs of normal dogs at about a constant time, seventy-two hours. It is a coincidence of import that the physiological death which we have been studying usually takes place in about the same time as is necessary for stoma drainage to begin. Thus we have come to regard the cutting out of the stoma as a sort of index of resistance of the individual to the intoxication process, and we have proceeded to create different degrees of toxicity, which we found we could do by varying the position of the obstruction and of chronicling the results in terms

of gastric drainage. For it should be noted that almost any form of drainage, whether through the normal channel of the gut, or abnormally through the stomach or even through an entero-anastomosis of the aboral loop with the oral loop, will counteract the lethal effects of what we believe to be a physiological death, due to a disturbance of physiological intra-enteric enzymotic balance.

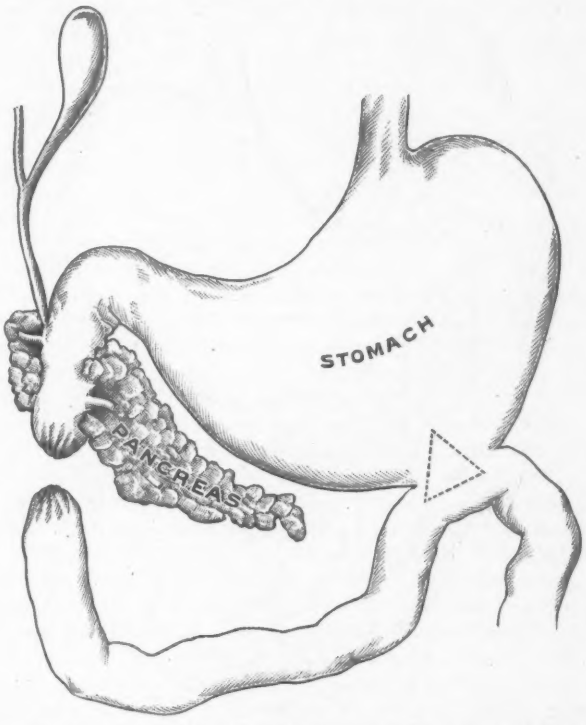

FIG. 1.—Duodenal obstruction; twine triangular control. In this class of experiments the bile and pancreatic fluid do not drain. Death before stomach drainage almost invariably occurs irrespective of the presence or absence of food in the stomach. This short-loop type should be given retrograde lavage or anti-enzyme serum from the long-loop class.

DETERMINATION OF ABORAL LETHAL LINE FOR PHYSIOLOGICAL DEATH. Logically the first step after determining by a long series of experiments that death followed the closure of the duodenum before drainage became established through the triangular stoma, was to ascertain the effect of practising a similar technique, but modified by placing the obstruction in the jejunum (Fig. 2). Another lengthy series of experiments determined, I believe with reasonable accuracy, that death would not occur in a medium-sized dog until

after the free drainage of the stomach, that is, several weeks, in any case when the obstruction lay more than 35 cm. aboral to the pylorus. This distance probably varies somewhat according to the size of the dog. The individuals exposed to this type of experiments will in future be referred to as the "long-loop dogs." For to them on account of the possible production of anti-enzymes, or protective

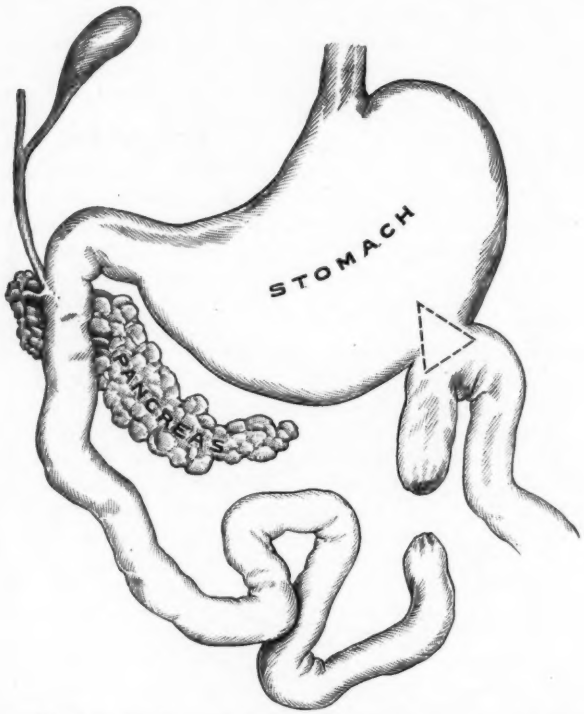

FIG. 2.—Jejunal obstruction. The length of the oral loop was more than 35 cm. In this class of experiments the dog lives until the twine cuts the stoma and often for months thereafter. Obstruction between this (35 cm.) and the greater pancreatic duct is almost always fatal before gastric drainage begins. Does the intestine detoxicate by the addition of an anti-enzyme, or does it save life by offering a larger field for absorption, thus diluting the toxic elements? This long-loop class may furnish a protective anti-enzyme serum for use in the short-loop class.

bodies of unknown character, there attaches a particular and perhaps a lasting interest. These long-loop dogs, barring ordinary accidents, survive the moderate toxemia to which the obstruction gives rise and will live often for several months without apparent discomfort or loss of body function. On autopsy, the oral segment was found to be but moderately dilated, as a rule, and the evenness

of digestive function suggested the phenomenon of gastro-proteid digestion. But the theoretical considerations which offer themselves as a result of this particular group of experiments must not interfere with this chronicle of plain observed facts.

Determination of Oral Lethal Line for Physiological Death. The next step naturally was to determine the oral limits of the point of obstruction beyond which one might go and not encounter physiological death within the time limit of triangular control. Because of the studies of Roger upon the gastrotoxins, and of the recent publication of Bolton describing a gastrotoxic serum, it is of very great importance to know whether the lethal bodies take their origin from the gastric mucosa, from the pancreatic fluid, or from the duodenum. Roger states that simple ligation of the pylorus leads to this physiological death in from seventy-two hours to five days. That, it will be observed, is just without the limit of the twine triangular time control. It is true that Roger did not employ the delayed gastro-enterostomy for a control, and so much that is accidental is certain to enter into all this sort of work that one feels hesitancy either in commenting upon the results obtained by others or impressing one's own experimental findings. It is true, however, that we have observed this fact: Given free drainage of the duodenum through the normal channel, as shown in Fig. 3, the stomach may be obstructed at or near the pylorus more frequently without lethal result until the cutting through of the triangular stoma than if the obstruction were in the duct-bearing portion of the duodenum. Of course, in this type of experiment, with the cutting through of the stoma, there ceases at once to be a reason why the animals should not live for an indefinite period. I do not wish to be understood as saying that no physiological toxic elements arise from the stomach and that the source of the toxicity is strictly duodenal or pancreatic; but we have been struck by the fact that, discounting all consideration of biliary toxemia, which one seems quite justified in doing, at least the chief source of the poison is either in the duodenum or the pancreas. In the light of our present knowledge, and measuring the degree of toxicity by our time drainage unit, rather than attempting to measure it, as Roger has done, in terms of toxic units, we were led to assume that the source of the toxemia was not in the stomach but in the duodenum. This enabled us, for purposes of study, at any rate, to place the oral limit of the lethal line between the pylorus and the papilla of Vater, because until now the question of the influence of the bile has not yet been worked out.

The duct-bearing portion of the duodenum has long been recognized as an area having unknown and profoundly complex physiological properties, and it is in part the object of this paper to demonstrate that the most accurate interpretation and knowledge of the physiological processes going on in this short tube must form

the groundwork for future therapeutic progress, be it surgical or medical; not alone on the alimentary canal, but as one should logically expect, as well upon its great glands, the liver and the pancreas. The morphological relationship of the stomach, liver, and pancreas to the duodenum has been graphically portrayed by Mumford, who says that the pancreas, the liver and ducts, and the stomach hang like three apples on a single stem, the duodenum. Whatever affects one often affects the others. What more striking

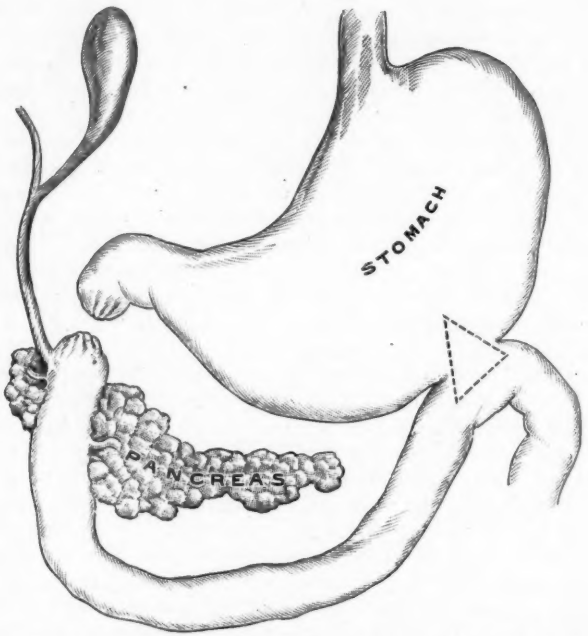

FIG. 3.—Duodenal obstruction; twine triangular control. Both the pancreatic fluid and the bile empty into the aboral loop. In this class of experiments there is usually no fatal outcome during stoma control, even if the stomach contains food at the time of the operation.

simile could one have? I submit that our studies have carried us still farther and that we are justified in considering not only the morphological relations, but the physiological relations as fixed. Is it not significant, in view of the close morphological relationship of these organs, that we have from unknown causes fatal hemorrhages into the pancreas, fatal dilatation of the stomach, fatal sequels to biliary operations which are not properly drained? I leave the discussion of this to those present more qualified to speak of it than I, and continue with the narration of our experimental observations.

Elimination of the Bile by Duct Ligation; Cholecystenterostomy and Transplantation of the Point of Discharge Into the Duodenum. A long series of experiments, painful to the operator in point of technical detail, was created by which the bile was intended to drain into the ileum by the use of the ordinary suture opening between the gall bladder and the gut. For some reason, however, although the technical part was accurately executed, there

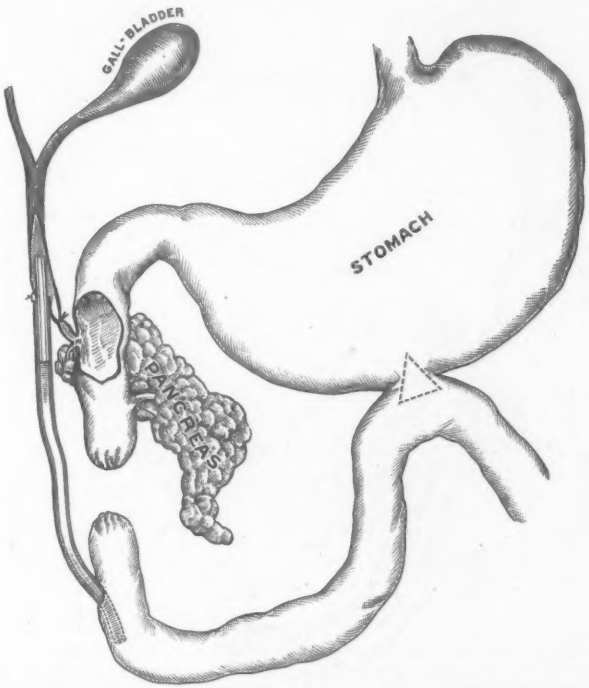

Fig. 4.—Extra-enteric transposition of the biliary secretion (Sullivan's technique). A glass cannula is inserted in the common bile duct; a rubber tube over the glass is stitched to the cut margin of the duct and introduced within the gut aboral to the intestinal obstruction. The bile duct is tied at the entrance to the duodenum.

was in every case a failure of the bile to drain. We finally concluded that there was either a change in its composition, owing to infection from the ileum, or that the secretory function of the liver cells had been abandoned or changed to an absorptive one. In any event, the bile draining or not draining, it was not possible for it to enter the oral loop, as the common duct had been ligated and divided, but the results, so far as the physiological death went, were the same. Death occurred in short-loop dogs before stoma-control

drainage. To fortify the position and to enable us to feel that we were not superimposing hepatic changes upon those under consideration, Mr. Arthur Sullivan, the senior laboratory assistant, devised means for the direct transplantation of the bile (Figs. 4 and 5). It comprises the reconstruction of the common bile duct, and will form the basis of a communication from him at a later date. The use of this simple and effective technique allowed of sufficient room between

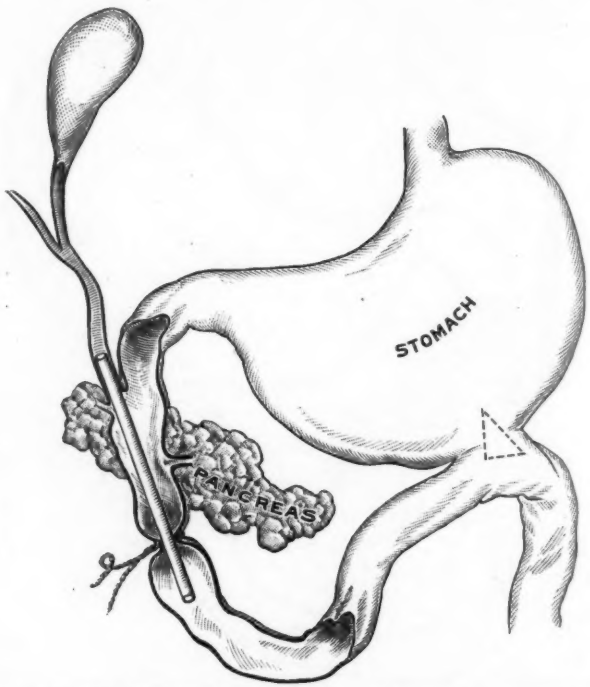

FIG. 5.—Intra-enteric transposition of the biliary secretion; twine stoma control. The forepart of the gut is shaved off to show the tube in position. This technique is difficult of execution and is further objectionable in not permitting actual section of the gut at the point of obstruction. There is apt to be leakage of the intestinal contents around the tube. This vitiates the experiment.

the transplanted biliary intake and the greater duct of the pancreas, either for complete section and invagination of the duodenum, or its ligation, as the case might be. Here, again, a sufficient series of experiments demonstrated that the supposed toxicity of the bile, at least in regard to obstructive death, was erroneous. It did not matter whether the bile emptied into the oral (Fig. 6) or aboral loop near the point of obstruction, whether the duct was simply ligated and cut, or whether cholecystileostomy was done, the lethal

outcome appeared rather conclusively still to be dependent entirely upon the position of the obstruction. In other words, bile, the salts of which are known to possess a very measurable degree of toxicity, was in no way connected with the physiological death under observation.

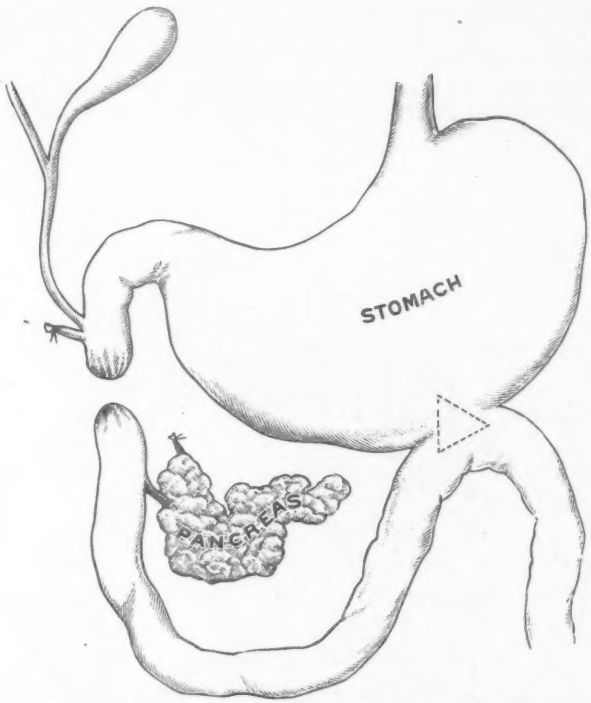

FIG. 6.—Duodenal obstruction between the pancreatic ducts; twine stoma control. The duct of Wirsung is tied and cut so that bile alone enters the oral loop. Drainage of the pancreas by the greater duct is adequate to prevent undue hardening or fat necrosis. The gland continues macroscopically in good condition. Dogs usually live during the period of stoma control

RELATION OF THE PANCREATIC SECRETION TO INTESTINAL OBSTRUCTIVE PHYSIOLOGICAL DEATH. The morphology of the parts does not allow a transposition of the pancreatic secretion, in the first place, because there are two ducts, and in the second place, because they are very short and firmly fixed to the pancreatic tissue (Fig. 7). Any interference with this, no matter however delicate, may lead to fat necrosis and other conditions which confuse the point of issue. By using Sullivan's tubes, however, we were able to move the point of entry of the bile as many centimeters aboral to the papilla of Vater as was convenient. After ligating the lesser

duct at its point of entrance beside the papilla and cutting it, we could make certain of having sufficient room to sever and invaginate the duodenum in such manner that all the pancreatic secretion might enter into the oral or the aboral loop. Opie has commented on the fact that drainage of the greater duct would usually suffice to prevent any undue hardening of the pancreatic gland because of retained secretion, and we have been glad to make use of his observation by tying and cutting the lesser duct. The result of these studies was conclusive in one regard: irrespective of the whereabouts of the discharged bile, the dogs lived during stoma control

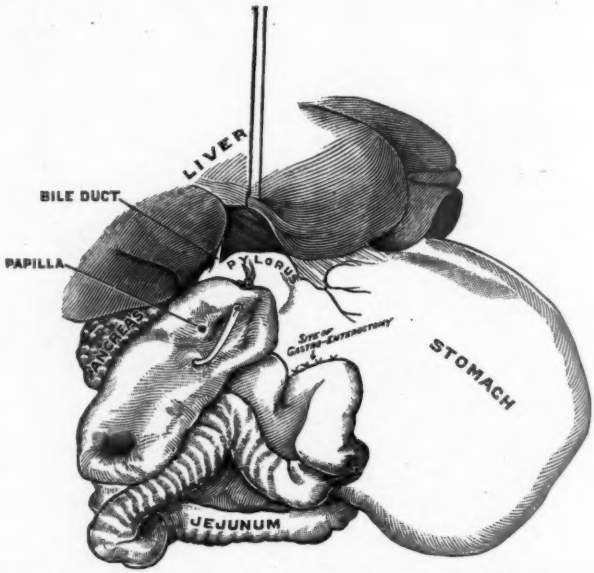

FIG. 7.—Attempted transposition of the pancreatic secretion oral to the duodenal obstruction produced by a ligature. The bile drains aborally. The lesser pancreatic duct is ligated.

when the pancreatic secretions drained aborally, and they died during stoma control when it was confined in the oral loop. I ask that this be not interpreted too positively, because enough conclusive work has not yet been done to justify too positive conclusions. This may well be pardoned, because of difficulties arising from the excessive sensitiveness of the duct-bearing portion of the duodenum, but we have gone far enough to justify our asking for corroborative evidence from others.

We understand that the secretions of the gastric mucosa may be toxic and that this toxicity may be increased many thousands of

times by an oral intestinal obstruction, but we have accomplished enough strongly to suggest at any rate that, whatever may be the nature and degree of this toxemia, a toxemia which develops from a disturbance in the duct-bearing portion of the duodenum contains poisons of a much graver nature. It is presumably not to be

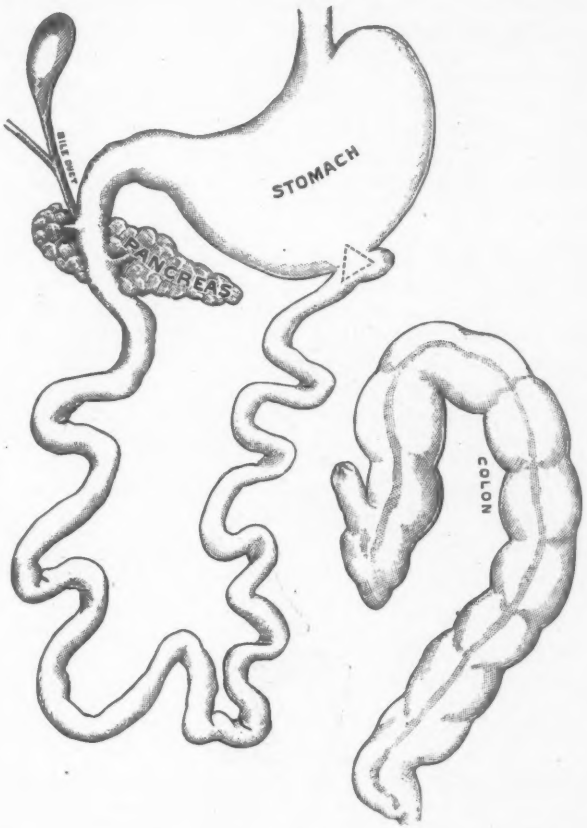

FIG. 8.—The entire small intestine forms the loop. The dogs lived several weeks.

denied that the increase in amount of gastrotoxins noticed after pyloric obstruction may well be brought about by the interference of a normal duodenal limitation of such toxin development. It is a point of perhaps more than academic interest that Weinland has found an antitryptic ferment to exist in the oral portion of the small intestine. Is one justified in supposing that, as the pancreatic

juice, grossly at least, appears to be the lethal agent, the danger from intestinal obstruction grows less and less the farther one places it from the pylorus, and therefore more and more in the antitryptic bearing portions of the canal, and this because of zymotic action. I do not wish to be understood as stating or even suggesting that trypsin alone or as such is responsible for the phenomena; no doubt there are many other ferments and antiferments occurring in the duct-bearing portion of the duodenum, but I speak of the

FIG. 9.—Retrograde lavage in a dog. This removes the toxic duodenal products quicker and more thoroughly than ordinary lavage.

trypsin simply as a representative of the class, because I understand its antibody to have been definitely found. It may indeed be that there is some form of internal secretion produced by the duodenum, possibly not directly associated with the processes of digestion, which is the fundamental factor in causing this physiological form of obstructive death. This should be capable of demonstration by experimental methods. Some such hypothesis is at present necessary in order to explain the singular phenomenon of the protective

power of the first 35 cm. of the intestine, the presence of which in the oral loop sufficing to prevent death before the opening of the triangular control. It may also explain the curious conditions shown in Fig. 8.

THERAPEUTICS. So far the suggestions as to treatment for these dogs have been based upon the belief that we had shown the region of maximum toxicity to be the duodenum rather than the stomach. It seemed, therefore, logical to irrigate the entire region rather than the stomach alone, and this by a sort of retrograde flushing (Fig. 9). This in a dog is easy to accomplish, the pyloric sphincter offering no obstruction either to alkaline or to acid irrigation. It is conceivable that some modification of this method might possibly be employed upon the human being, for constant irrigation of the duct-bearing portion of the duodenum would seem on experimental grounds to be the one logical method of preventing the absorption of the physiological poisons referred to.

A more philosophical method of meeting the conditions might be to transfuse the sick short-loop dog from a long-loop dog, which may be supposed to have manufactured, in the course of his temporary illness occurring before the establishment of gastric drainage, certain antibodies which might be protective to the short-loop dogs. We have done a little work in transfusing the long-loop into the short-loop dog, and have noted improvement in the latter; but this might come from accumulation of the fresh blood rather than from the presence of anti-enzymes. We are, therefore, endeavoring to obtain a serum from the long-loop dog, with which we hope to tide the short-loop dog over his period of hypertoxicity, so that he too may live until the triangular control gives gastric drainage and assures permanent life.

REVIEWS.

MODERN MEDICINE. ITS THEORY AND PRACTICE. In Original Contributions by American and Foreign Authors. Edited by WILLIAM OSLER, M.D., Regius Professor of Medicine in Oxford University, England; Assisted by THOMAS MCCRAE, M.D., Associate Professor of Medicine and Clinical Therapeutics in the Johns Hopkins University, Baltimore. In seven volumes. Volume V; pp. 903. Philadelphia and New York: Lea & Febiger, 1908.

VOLUME V of Osler's *Modern Medicine*, which is devoted to a discussion of the important subject of diseases of the alimentary tract, contains several notable contributions, particularly those on functional disorders of the stomach, by Julius Friedenwald; on organic diseases of the stomach, by Charles F. Martin; on diseases of the intestines, by Alfred Stengel; and on diseases of the peritoneum, by Humphry Davy Rolleston. The volume opens with a short introductory chapter by Charles G. Stockton on certain critical relations that may exist between disturbed physiological activity and structural changes. This comprises, among other matters, a discussion of the inter-relations and the adaptability and vicarious action of the digestive functions, the nature of the functional disturbances of digestion, the functional disturbances in relation to structural disease and structural changes resulting from functional disorders, infection in relation to digestion, disharmonies of secretion, the significance of the digestive juices and of the intestinal flora, and the influence of psychoneuroses on digestion—all of which, though briefly, is excellently told and serves well to introduce what follows.

Major interest centres in the description of diseases of the stomach. Dr. Friedenwald's seventy pages are all too few to allow of a thorough discussion of the protean manifestations of the so-called gastric neuroses, but what he says is eminently practical and to the point. Adopting Boas' classification of these neuroses into the monosymptomatic (comprising the irritative and the depressive group) and the polysymptomatic (nervous dyspepsia), he analzyes critically 1592 cases. C. F. Martin expresses the opinion that gastric ulcer has as its main etiological factors a destruction of the gastric epithelium, disturbance of the circulation in the stomach, and acidity of the gastric juice, the combination permitting autodigestion; but he seems not to have been able to adduce any conclusive evidence of the real cause of the necrosis, nor could any of us. As regards treatment, he prefers starvation or very little food for a time; he lays stress upon the necessity of care in the transition stages from a liquid

to a semisolid diet; and he says that examination of the feces for occult blood is an excellent guide for the transition to more generous diets. He regards surgical treatment indicated in chronic gastric ulcer that resists medical treatment for two months, in those cases that cause mild dyspeptic symptoms for a prolonged period and then culminate in hematemesis, and in chronic recurring ulcers even when each attack lasts only a comparatively short time. Unfortunately Dr. Martin has been unable to add much that will aid us in the early diagnosis of carcinoma of the stomach; but at present this may be said to be inherent in the nature of the disorder. In case reasonable suspicion of the disease exists, he advised exploratory operation to make, not to confirm, the diagnosis. The entire chapter of 152 pages on the organic diseases of the stomach is quite worthy of its author.

Dr. Stengel's chapter of 168 pages is an excellent summary of existing knowledge on the diseases of the intestine, tempered by the personal experience of the author. The introductory statements on physiological subjects are opportune and may be read with interest and profit. The diarrhœic disorders are well described, and so also is constipation, although perhaps it would not have been amiss to have discussed in some detail the spastic constipation of some writers. The thirty-two pages devoted to appendicitis will repay the reading. The lesions are well described, although they are assumed to begin practically always in the mucosa—an opinion subject to modification in view of some recent work on the hematogenic source of the infection in some cases; the symptomatology and diagnosis are accurately portrayed; and as regards the treatment, it is said that, eliminating certain exceptional cases, the only proper treatment of acute appendicitis consists of immediate or prompt operation. But the exceptional cases include some that "will be regarded by both the physician and the surgeon as proper cases for non-operative treatment;" and here's the rub. Many of Dr. Stengel's brethren would have welcomed his own explicit opinion regarding the exact nature of these cases, as well as definite statements concerning the indications for operation from the point of view of the physician.

Humphry Davy Rolleston's 104 pages on diseases of the peritoneum are such as one naturally expects of their distinguished author. His discussion of the causes, nature, and types of ascites and of the acute and chronic forms of peritonitis are fully abreast of advanced knowledge, and faithfully reflect all that is really known of the subjects.

The aforementioned contributions on diseases of the stomach, intestines, and peritoneum comprise more than one-half of the volume; but there are other valuable although shorter communications. David Riesman contributes a chapter on diseases of the mouth and salivary glands. Attention is directed to the importance of septic

infection of oral origin and to the often overlooked fact that disease of distant organs (ulcerative endocarditis, pernicious anemia, etc.) may originate in bacterial infection of the mouth. The common forms of stomatitis are well described, as well as the changes in the mouth due to general diseases, such as typhoid fever, uremia, diabetes, pyorrhœa alveolaris, etc. The chapter is embellished by five excellent colored plates. John McCrae contributes a short chapter on diseases of the œsophagus, giving due emphasis, among other matters, to the importance of radiography with bismuth pastes in the diagnosis of diverticula and dilatation. Thomas R. Brown contributes 22 pages on splanchnoptosis (Glenard's disease), in which he accentuates the importance of a definite congenital defect as the underlying cause of the disorder in many cases, minimizes the significance of nephroptosis *per se*, and states that in the vast majority of cases the disorder is strictly medical and surgical only when the symptoms are so definitely referable to one or two organs that their suspension offers a good chance of the disappearance of the symptoms. Eugene L. Opie contributes a chapter of 62 pages on diseases of the pancreas, which is a reflection of the well grounded views of a pioneer worker in the subject. Emphasis is placed upon the significance and importance of changes in the islands of Langerhans in diabetes; but the absence of some discussion of the diagnostic significance of the Cammidge reaction in disease of the pancreas is noteworthy and somewhat to be deplored. A. O. J. Kelly contributes the concluding chapter of 174 pages on diseases of the liver, gall-bladder, and biliary ducts. One may perhaps venture the opinion that the less said about it the better. A. K.

THE SURGERY OF THE UPPER ABDOMEN. By JOHN B. DEAVER, M.D., Surgeon-in-chief to the German Hospital, Philadelphia, and ASTLEY PASTON COOPER ASHHURST, M.D., Surgeon to the Out-patient Department of the Episcopal Hospital, Philadelphia. In Two Volumes. Volume I, Surgery of the Stomach and Duodenum. Pp. 468; 76 illustrations. Philadelphia: P. Blakiston's Son & Co., 1909.

THE region of the upper abdomen presents problems for diagnosis and treatment of the greatest interest to the practitioner and the surgeon, more so perhaps than any other region of the body, because here reside the organs essential to digestion. Any disturbance of their anatomical relations, any disease causing perversion of their physiological functions, reacts upon the organism as a whole and profoundly affects the metabolism of the body. It seems fitting,

therefore, that a special treatise should be written upon the stomach, duodenum, liver and bile passages, pancreas, and spleen, if it presents the affections to which these organs are subject in a modern and scientific manner. The volume before us comprises the surgical lesions of the stomach and duodenum described by two surgeons who combine an experience and operative dexterity of the highest order with the ability to sift the writings of others with excellent judgment. The book contains 15 chapters, describing the anatomy, physiology, benign and malignant affections, operative technique, and incidental complications of the diseases in questions.

The chapters upon the anatomy are excellent; anatomical matters are discussed as a whole, instead of the surgery of each organ being prefaced by a brief anatomical outline with its attendant repetitions. The physiology of digestion is well worked out and presents a good digest of the writings of Pawlow, Starling, Kelling, Cannon, and others. In discussing the etiology of gastric ulcer the authors believe that the continued study of normal physiology, together with the "living pathology" observed at the operating table, will probably determine, in the near future, the factors concerned in the production of this disease. We venture to assert, however, that progress in this direction is much more likely to be made in the experimental laboratory than in the clinical amphitheater. The entire subject of gastric ulcer is discussed broadly and thoroughly; in vigorous terms the attention of the medical man, who has cases of chronic gastric indigestion under his care, is called to the advantages of modern surgical treatment. It is unfortunate that Patterson's statistics are made use of, because, while he found less than 7 per cent. of 116 patients whose condition was unsatisfactory after operation, he was only able to trace 116 out of 247 patients to whom he sent inquiries; who knows the condition of the other 131 patients? Some attention might have been paid to the postoperative treatment of the ulcer cases, as but few observers will agree with the quotation from Kocher (p. 107) that "the patient does not require to pay any further attention to the nature of his food." All of the benign affections of the stomach are discussed in an able and interesting manner, including pylorospasm, dilatation, gastroptosis, hour-glass contraction, infantile stenosis of the pylorus, etc. Gastrojejunostomy is preferred to gastropexy in the treatment of gastroptosis, and the purely functional origin of pylorospasm is denied.

The difficult but important subject of gastric carcinoma is considered in 32 pages, and while nothing is offered to contradict our impression that in spite of an array of statistics this is a nearly hopeless disease from the standpoint of treatment, yet the topic is made interesting by the authors. The usual emphasis is laid upon chronic dyspepsia as the chief predisposing cause of gastric carcinoma and upon the fact that under medical treatment all patients will die in about twelve months unless the skilful surgeon steps in and

saves many lives otherwise doomed to destruction. It is gratifying to note the reduction in the primary mortality after gastrectomy, and that about 10 to 15 per cent. of patients treated by gastrectomy are said to be permanently cured. While it is true that excision following a diagnosis made in the incipient stage, or during the time, according to Menetrier's fanciful theory (p. 271), when an ulcer is progressing to the adenomatous stage, would in all probability always result in a cure, yet the ability to make such a diagnosis does not seem at present to be possible. The human race will immortalize the man whose research shows the exact method of cancer dissemination or who can devise a test whereby the tissue juices or blood will indicate that carcinomatous transformation is taking place.

The chapters upon the technique of operation and upon the complications and sequels are excellent, the index is sufficiently comprehensive, and an index of names adds to the usefulness of the volume. The authors are to be congratulated upon having produced a monograph furnishing accurate information upon every subject connected with the stomach and duodenum that may be amenable to surgical treatment. One cannot refrain from commenting upon the pedantic method of spelling *develope*, *clinique*, *elabourate*, etc. G. P. M.

GYNECOLOGY AND ABDOMINAL SURGERY. Edited by HOWARD A. KELLY, M.D., F.R.C.S., Professor of Gynecologic Surgery in the Johns Hopkins University, Baltimore, and CHARLES P. NOBLE, M.D., S.D., Clinical Professor of Gynecology in the Woman's Medical College, Philadelphia. Volume II. Pp. 862; 871 Illustrations. Philadelphia and London: W. B. Saunders Co., 1908.

WE had the pleasure of reading the first part of this work for review, and took occasion at that time to congratulate the authors upon the splendid contribution to medical literature which it represents. We are, if possible, more enthusiastic in regard to this, the second portion of the work. As is at once apparent, upon even a cursory examination, the present volume is true to its title and does not limit itself to the field of pelvic surgery. The editors advocate strongly that all men who open the abdomen shall be equipped to perform any operation demanded by the conditions present. There can be no possible criticism of their position, since no man can tell with certainty how many or what variety of complications may be met within the abdomen, and, therefore, no one can be considered a safe operator who is unable to cope with any condition possibly existent between the diaphragm and the pelvic floor.

The volume opens with a chapter of 78 pages by G. Brown Miller

upon the complications following operations, in which every possible condition is mentioned and those of importance carefully considered. The author has omitted to mention, in the prophylaxis of phlebitis, the new and radical practice of getting patients out of bed one or two days after subjection to major surgery; upon this omission he is to be congratulated. The chapter upon the Cesarean operation, contributed by J. F. W. Ross, is hardly a satisfactory exposition in the light of present-day experience. His statement that "Those who have performed Cesarean section will be most reluctant to consent to the induction of premature labor" must be adversely criticised. How many of us in our own family would consent to the abdominal delivery, if premature labor, two or at the most three weeks before term, gave good promise of a living child? We must certainly differ as to the advisability of ever instituting drainage in a clean case. Certainly most operators have now given up the use of the elastic cervical temporary ligature. It is most decidedly an exaggeration to say that an incision through the placenta, in incising the uterus, brings the operator "face to face with all the features of placenta prævia;" it would be fortunate, indeed, if the latter condition were as easily controlled as the former slight complication. The method of closure of the uterine wound advocated by the author is incomplete in that the use of a double-tier suture of buried catgut in the myometrium is omitted. Finally, the reversion to the old practice of abdominal binders "for some months after operative recovery" is not impressive.

Richard C. Norris, in a chapter of ten pages, considers the important subject of the operative procedures which may be required during the course of pregnancy for accidental complications. In his consideration of appendectomy he quotes Hirst's advocacy of the Cesarean operation after the seventh month of pregnancy, because of the difficulty of returning so large a uterus to the abdominal cavity. The operative treatment of sepsis in the child-bearing period, contributed by B. C. Hirst, is a concise statement of the opinions of the author. His recommendation in favor of instrumental exploration and evacuation of the uterus will be questioned by some good authorities, probably because the abuse of the method is too often mistaken for its proper use.

J. Whitridge Williams contributes a most scientific exposition of extra-uterine pregnancy. At the end of the chapter of over forty pages he has added a very complete bibliography. We are glad to note that the menstrual history is given second place in the symptomatology of the condition. His opinion that, so far, no single case has ever been reported affording indisputable proof of the occurrence of primary abdominal pregnancy, will meet with disapproval upon the part of some capable men. The chapter upon the diseases of the female breast, by J. C. Bloodgood, is one of the most noteworthy in the whole work. It is based upon a clinical and pathological study

of 1048 specimens obtained for the most part from the clinic of Professor Halsted; it comprises almost one hundred pages, is well and profusely illustrated, and is most painstaking in its attention to the minutiæ of the subject. The definiteness of statement regarding the duties of the physician as well as of the surgeon is very timely. Albert J. Ochsner, in his consideration of operations upon the gall-bladder, bile ducts, and liver, leaves nothing to be desired, and the same is true of the next succeeding portion of the work upon operations upon the stomach, by B. G. A. Moynihan.

John B. Murphy, in a chapter of over 120 pages, gives a complete consideration of the subject of intestinal surgery. Our only criticism is that the incorporation of a detailed description of the various illustrations of intestinal suture would have been better than depending upon illustrations alone to convey the needful teaching. The chapters on operations for diseases of the vermiform appendix, by Howard A. Kelly and Elizabeth Hurdon, surgery of the pancreas, by Eugene L. Opie, and operations upon the spleen, by Howard A. Kelly, are impressive of the pregnant possibilities of the next decade.

With the space at our command it is manifestly impossible to present an adequate review of this work. All that we can hope to have accomplished is that by commenting upon certain features and by suggesting the scope of the subjects we may have given to the reader an intelligent idea of the extent of the work. From the time of our first knowledge that this book was in preparation, we have waited with impatience for its completion. There can be no question that it will have as favorable a reception as its great merits warrant. W. R. N.

THE PRINCIPLES AND PRACTICE OF GYNECOLOGY. By E. C. DUDLEY, A.M., M.D., Professor of Gynecology in the Northwestern University Medical School, Chicago. Fifth edition; pp. 806; 431 illustrations and 20 full-page plates. Philadelphia and New York: Lea & Febiger, 1908.

THE work before us, in its fifth edition, can hardly be said to need a review, as the profession has definitely decided as to its merits by enabling the publication of the several editions. It is needless to say that the subject of gynecology has received adequate treatment. The author has made two additions in the present volume: one an introductory chapter and the other a chapter upon incontinence of urine in women. The first of these is one which we wish read by all gynecologists, as a means of encouragement to the further prosecution of their work, and by all general surgeons as an antidote to presumption. The author justifies the existence and perpetuation

of gynecology both by history and prophecy. The other chapter consists of but three pages, and is introduced to explain an operation for the advancement of the external urethra as a means of cure in conditions of incontinence of a non-inflammatory nature. His method consists in an inverted U-shaped denudation of the vestibule, with closure by catgut sutures. If efficacious it will certainly be a most important addition to the means of treatment of this very obstinate condition. Otherwise, with certain minor changes, and a considerable amount of revision, the book is unchanged. In our opinion it is one of the most satisfactory expositions of the subject of which we have knowledge.

There are of course some points upon which men of experience differ from the views set forth by the author; as, for instance, in his chapter upon cystoscopy it seems to us a pity that the Casper and Nitze models should be the only ones figured. We simply make this statement as an example of the only variety of criticism to which this book lends itself. In other words, any adverse criticism would simply be the exploitation of the personal opinions of the writer, and, therefore, according to our conception of the proprieties of review, has no place. We would call especial attention to the chapters upon the repair of perineal lacerations, because of the excellence of the illustrations as well as the letter press, and we are glad to note that the author is not an advocate of the immediate repair of lacerations of the cervix, or even their repair within a few weeks of the delivery. He believes that better results are to be obtained by operating some three months later. We are also very glad to find that his opinion of ventrosuspension has not been changed by the present fashion of performing all such operations through the medium of the round ligaments. His attitude is that, while fixation is wrong in the reproductive period, the operation which has for its aim the suspension of the uterus to the anterior abdominal wall by an artificially formed ligament, should not yet be cast away. He states that hysterorrhaphy properly performed gives more security against recurrence of displacement than any of the ligament-shortening operations. He nevertheless gives a full account of the Alexander and Gilliam operations, with a modification of the latter which seems to us to promise well. He prefers the last-mentioned method in his own work, except in selected cases, in which he still does the suspension from the abdominal wall.

Any attempt further to indicate the subjects discussed would simply result in the incorporation of the table of contents; suffice it to say, that the whole subject of gynecology is carefully covered, but that the author stops there and does not treat of conditions of the upper abdomen. In this we believe him to be wise, since, although the upper abdomen is properly within the province of the gynecological operator, there is a distinct benefit in the limitation of text-books to the old lines. W. R. N.

GENERAL SURGERY. A PRESENTATION OF THE SCIENTIFIC PRINCIPLES UPON WHICH THE PRACTICE OF MODERN SURGERY IS BASED. By EHRICH LEXER, M.D., Professor of Surgery in the University of Königsberg. American edition, edited by ARTHUR DEAN BEVAN, M.D., Professor and Head of the Department of Surgery in the Rush Medical College in Affiliation with the University of Chicago. An authorized translation of the second German edition by DEAN LEWIS, M.D., Assistant Professor of Surgery in the Rush Medical College in Affiliation with the University of Chicago. Pp. 1041; 449 illustrations and 2 plates. New York and London: D. Appleton & Co., 1908.

THIS translation of a successful German text-book on surgery will be cordially welcomed by the profession in this country. Prof. Lexer is well known here, particularly for his remarkable achievements in the surgery of the bones and joints, and it will be a pleasure to those who do not read German with facility to become acquainted, through Dr. Lewis's admirable translation, with the views and the teachings of one of the foremost of continental writers.

The volume, which deals solely with general surgery, is divided into seven parts, as follows: Part I, which includes: (1) Wounds, their treatment and repair; (2) aseptic technique; (3) general and local anesthesia; (4) general principles of plastic operations. Part II. Wound infections and surgical infectious diseases: (1) The nature of infection, local and general reaction; (2) wound infections caused by pyogenic and putrefactive bacteria and their results; (3) wound infections of different origins and surgical infectious diseases. Part III. Necrosis. Part IV. Injuries of soft tissues, bones, and joints, and their treatment: (1) Mechanical injuries; (2) chemical injuries; (3) thermal injuries; (4) general results of injuries. Part V. Important surgical diseases, excluding infections and tumors: Diseases of the skin, etc., muscles, tendons, bloodvessels, nerves, joints, and bones. Part VI. Tumors. Part VII. Cysts. There are also two appendices to the American edition: the first, on direct transfusion of blood, is an abstract of Crile's work; while the second, on opsonins, phagocytosis, and therapeutic inoculations of dead bacteria, has been contributed by Dr. Rosenow.

When an English-speaking professor of surgery candidly admits that he can find no text-book in his own language to suit him, and, instead of supplying the deficiency by one of his own, deliberately adopts a German volume as the standard of instruction for his students, he in a measure challenges criticism of his judgment of American and English text-books in general, and of his selection of the particular volume now before us for review. No apology, we believe, is needed for Dr. Bevan's high appreciation of the value of a training in the principles of surgery before the study of the practice of this art is begun; but we certainly think it doubtful

whether cramming so much theoretical knowledge down the throats of medical students at one meal, as it were, without any accompanying jam in the nature of clinical application of the theories expounded will not rather produce a disgust for further study than an eagerness to learn more. In other words, we believe this volume contains an unnecessary amount of matter for the third-year student, for whose use it is designed; and that the rather unpalatable form in which the pabulum is served will tend to make the acquisition of a knowledge of surgical principles more difficult for the student, instead of easier, which should be the aim of every teacher. Particularly useless to the American student are the long lists of bibliographical references, almost exclusively to German literature, which have been transferred in bulk from the German edition. Even when rare references are made in the text to the work of an English, French, or American writer, it is the exception for the bibliography to contain his name. To such an extent is this Anglophobia carried that even the editor's own suggestions are expounded in German at p. 315.

A text-book on surgery may be criticised, first, as to inclusiveness and exclusiveness; second, as to arrangement of subject matter. There are included in this volume some topics which really belong to general medicine, and which seem decidedly out of place in a text-book on surgery. Mention may be made of diphtheria, to which ten pages are devoted, as an example of lack of exclusiveness. Blastomycosis is discussed by Dr. Oliver Ormsby at a length of seventeen pages; surely this is a disproportionate amount of space to devote to such a topic, when only eight pages are occupied by local reaction to infection (inflammation), and less than seven pages to open wounds of bloodvessels, including the treatment of hemorrhage. Should Prof. Lexer adopt Dr. Bevan's suggestion that this chapter on blastomycosis be included in the next German edition, it is to be hoped that he will curtail it to a reasonable length. Among subjects which are slightly described or not mentioned at all are to be noted: Linen as a suture material; general anesthesia by ethyl chloride; the Matas operations for aneurysm (dismissed in four lines of text, though illustrated by eleven figures); and traumatic asphyxia, which is mentioned, though no name is given the condition; moreover, no notice is taken of the recent use of bismuth injections in the treatment of sinuses; a description of the use of x-rays and of skiagraphic examination for diagnosis is nowhere to be found; and there is no reference to the subject of traumatic delirium, unless it be included in the term "torpid and erethistic shock," which seems rather to correspond to what English and American surgeons, following the classical nomenclature of Travers, have long described as "prostration with excitement." Some of these omissions are excusable in the German edition, which dates from 1906; but they might well have been added by the American editor.

But the arrangement of the volume affords the chief ground for criticism. Here students are taught the treatment of wounds as the first lesson in surgery, not only before antisepsis and asepsis are discussed, and before the subject of wound repair has been learned, but even before the study of the local reaction of the tissues to injury has been described. It thus happens that the discussion (beginning at p. 35) of repair of wounds by "first" and "second intention" is mere gibberish until p. 146 is reached, where the local reaction to infection is described; and the causes of infection (bacteria) are not taught until p. 169, not only after the lesions they produce have been discussed, but considerably more than 100 pages after the subjects of asepsis and antisepsis have been concluded. This is a *hysteron proteron* with a vengeance! How can students be expected to appreciate the value of aseptic technique until they have been taught the pathology of infection?

These criticisms apart, the volume presents the subject of surgery in a very satisfactory manner, and with a wealth of original illustration which it would be difficult to surpass. A. P. C. A.

SURGICAL APPLIED ANATOMY. By SIR FREDERICK TREVES (BART.), Consulting Surgeon to the London Hospital. Fifth edition; Revised by ARTHUR KEITH, M.D., Lecturer on and Senior Demonstrator of Anatomy at the London Hospital. Pp. 640; 107 illustrations. Philadelphia: Lea Brothers & Co., 1908.

THIS volume is little in size only, as by the use of thin paper and small print a great mass of facts is compressed between its covers. The book has so long served as a *vade mecum* for students and practitioners of medicine that comment upon its field of usefulness or criticism of its contents would merely indicate a desire to try to find minor faults and differences in opinion inherent to any book. In the present edition the work has been revised and brought up to date, and the illustrations have been improved. The chapters upon the extremities are the best in the book, perhaps because in similar works the head and abdomen receive so much more attention. There are omissions from the anatomical standpoint, and some of the methods of procedure are clumsy, but the book succeeds in presenting the subject in a vivid, interesting, and sufficiently exact manner to make it most valuable as an introduction to the study of surgery, and as a guide to an intelligent and proper understanding, by the student, of the various surgical methods while he is engaged in ward duty. G. P. M.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Early Diagnosis of Pulmonary Tuberculosis.—HAUSMANN (*Deut. Arch. f. klin. Med.*, 1908, xciv, 595) was struck by the number of gastric cases in his practice which presented evidence of apical lesions. Those who raised no sputum he often sent to a lung specialist, and frequently his diagnosis of incipient pulmonary tuberculosis was reversed. Feeling that he was correct, he decided to examine the fasting stomach early in the morning for small particles of bronchial secretion. His first patient gave no history of cough, but had definite signs in one apex, his chief complaints being a feeling of fulness and weight in the epigastrium. A very small particle of mucus enclosing pus cells and lymphocytes and a few alveolar epithelial cells was obtained from the stomach, and when stained showed about ten tubercle bacilli in a field. In the last two months he has had six similar cases, all with the same result. He urges the usefulness of his method and suggests that some of the so-called "closed" or "healed" cases may be shown by this means to be in reality "open" cases of tuberculosis.

A New Clinical Test of Pancreatic Function.—E. ENRIQUEZ, L. AMBARD, and M. BINET (*Semaine méd.*, 1909, xxix, 13), note the importance of a knowledge of the function of the pancreas which may be gained by an estimation of the ferments lipase, trypsin, and amylopsin, especially if these can be regained totally from the stool. It is very difficult to do this with the first two, but the quantity of amylopsin can easily be determined. Previous work has shown that amylopsin is more abundant in diarrhœic stools. The authors in their research

on 150 subjects have evolved the following technique to obtain the maximum amount of amylopsin. To prevent the destruction of the ferment by trypsin, the person is first given some milk, about three-quarters of a liter, as the mixture of trypsin with the albumin will prevent its destructive action on the other ferments. A piece of ice is also placed in the vessel that receives the dejecta, to restrain microbic action. The unit used for expressing is the amount of sugar that can be formed in one hour by the total amount of the ferment (that is, sugar-gram-hour unit). The stool being diluted with water (20 liters), 1 c.c. of this mixture is added to 50 c.c. of a 1 per cent. solution of starch, acidified with HCl, and the whole incubated at 39° C. for half an hour. The amount of sugar produced is then determined quantitatively for this amount and so calculated for the total feces, the figures resulting giving so many amylopsin units. The amount of these units is fairly constant in healthy persons, but in two cases of carcinoma there was almost complete absence of amylopsin. The authors feel that further work along these lines and a more perfected technique will aid in understanding the function of the pancreas.

The Relation of Tetany to the Parathyroid Glands and to Calcium Metabolism.—W. G. MacCallum and C. Voegtlin (*Jour. Exp. Med.*, 1909, xi, 118) report the experimental work on this subject which they have been carrying on for some time, and conclude that there is an intimate relation between the various forms of tetany and the relative or absolute insufficiency of the parathyroid gland. These glands have a definite specific function. When extirpation of the parathyroids is complete, tetany appears, even in herbivora. Only a small amount of parathyroid tissue is required to prevent this. The effect of extirpation may be annulled by the re-injection of an extract of these glands, even from an animal of a widely different character. The parathyroid glands contain no considerable amount of iodine. In tetany there is apparently some disturbance of the composition of the circulating fluids, ordinarily prevented by the normal secretion of the parathyroid; this change in the composition disarranges the balance of the mineral constituents of the tissues. Calcium salts bear an important relation to the excitability of the central nervous system; their withdrawal leaves the nerve cells in a state of hyperexcitability, which can be made to disappear by supplying them with a solution of a calcium salt. Tetany may be regarded as an expression of hyperexcitability of the nerve cells from some such cause; the injection of a solution of a salt of calcium into the circulation of an animal in tetany promptly checks all symptoms and restores the animal to an apparently normal condition. Sodium and potassium, as well as some other salts that have been studied, have no such beneficial effects. This effect of calcium is of value in human therapeutics as a means of tiding over the period of acute parathyroid insufficiency until remnants of parathyroid tissue can recover their function or new parathyroid tissue be transplated. The metabolism in parathyroidectomized animals shows among other things a marked reduction in the calcium content of the tissues, especially of the blood and brain during tetany, and an increased output of calcium in the urine and feces on the development of tetany.

In general, then, the role of the calcium salts in connection with tetany may be conceived of as follows: These salts have a moderating influence upon the nerve cells; the parathyroid secretion in some way controls the calcium exchanges in the body. It may possibly be that in the absence of the parathyroid secretion substances arise which can combine with calcium, abstract it from the tissues, and cause its excretion, and that the parathyroid secretion prevents the appearance of such bodies. The mechanism of the parathyroid action is not determined, but the result, the impoverishment of the tissues with respect to calcium and the consequent development of hyperexcitability of the nerve cells and tetany, is proved. Only the restoration of calcium to the tissues can prevent this.

The Antitryptic Power of the Serum of Diagnostic Value.—L. AMBARD (*Semaine méd.*, 1908, xxviii, 532) notes that it has been known for some time that serum possesses the property of inhibiting the action of trypsin, thus checking the digestive power of the pancreatic juice. At one time this power was supposed to be of definite value in the diagnosis of cases of cancer, but later it has been found in other conditions. In animals this antitryptic power is increased by the injection of trypsin, and in man by the ingestion of pancreatin. This increased power and its compensatory hypersecretion forms a common link between cancer, nephritis, etc., and other conditions in which the antitryptic power of the serum is increased.

An Epidemic of Disease due to the Mouse Typhoid Bacillus.—FLEISCHANDERL (*Münch. med. Woch.*, 1909, lvi, 392) reports an epidemic of 20 cases occurring in his practice in April, 1908. The disease was characterized by a rapid onset with abdominal pain, followed in the next few hours by diarrhœa (eight to twenty stools in twenty-four hours), fever, and general malaise; the symptoms increased for two to three days, the temperature reaching 39° to 40° C.; in one case, vomiting, sharp abdominal pains, giddiness and staggering on walking occurred, and there was marked prostration; later, a rapid subsidence of symptoms and great lassitude for several days. In one case the convalescence was protracted through two weeks. The mild cases were without fever and all the symptoms were less severe. Fleischanderl thought of a paratyphoid epidemic, but, on inquiry found that Loeffler's mouse typhoid bacillus was being used in the locality to exterminate the field mice. His patients had aided in scattering bread which had been soaked in a suspension of mouse typhoid bacilli on the day preceding the onset of their illness. They had not washed their hands before eating, and thus there was every chance for infection. In the family of a teacher the father, mother, and one son were attacked, another son being unaffected. Inquiry developed the fact that all three had drunk milk from a pail which had previously contained bread and mouse typhoid bacilli suspension on the day before onset. The son who remained well had drunk no milk and had not distributed infected bread. The circumstantial evidence against the mouse typhoid bacillus was strong. Fleischanderl now infected himself by way of the alimentary tract. He was in perfect health, never had suffered from intestinal disorders, and had had no typhoid fever in his practice for over a year. Twenty-

two hours after infection he was attacked with mild abdominal pain, which soon became severe. Temperature and pulse remained normal. Three hours later diarrhœa began, and eight hours later he had a slight chill. His temperature rose to 38.7° C.; pulse, 106. He now had severe abdominal pain and prostration. At the end of thirty-six hours the temperature had risen to 39.2°, the pulse to 120. These symptoms lasted for forty-eight hours and then rapidly subsided, but left the patient in a depressed condition for two days longer. From his own feces as well as from those of some of the patients the bacillus of mouse typhoid was recovered in pure culture and proved by re-infection of mice. Serum from rabbits immunized to a laboratory culture of the mouse typhoid bacillus agglutinated not only the original culture, but also the various cultures obtained from the stools as well as the culture Fleischanderl used to infect himself. The agglutination was obtained in dilutions varying from 1 to 20 to 1 to 320. No agglutination occurred in controls or with the paratyphoid bacillus.

The Relation of Bovine to Human Tuberculosis.—W. L. Moss (*Johns. Hopkins Hospital Bulletin*, 1909, xx, 39) summarizes the literature on this important subject, and concludes that, while the circumstantial evidence points more or less strongly to the conception that human beings may be infected with tuberculosis from bovine sources, yet absolute proof is wanting. But the evidence that tuberculous cattle are a source of danger to man is so strong that on the basis of this alone it would seem advisable to take strict precautions against bovine tuberculosis. The economic losses among the cattle themselves, aside from any danger to man, are sufficiently great to demand a vigorous effort to stamp out bovine tuberculosis. The evidence furnished by autopsy statistics of primary intestinal tuberculosis reported by different observers is very complicated, and even if there was an agreement on its high incidence, this evidence could only be taken as circumstantial, since there is abundant opportunity for primary intestinal infection to occur with tuberculous material of human origin. The use of tuberculin from human and from bovine bacilli has not yet thrown much light on the question. The agglutination reaction does not seem to differentiate the two types of bacilli. It seems definitely established that there are two distinct types of tubercle bacilli, the human and the bovine, and that mutation from one type into another does not occur. The bovine type of bacillus has been demonstrated in 20 per cent. of the series of 306 cases among human beings. The bacillus which causes bovine tuberculosis may also cause tuberculosis in man, but infection need not be received directly from cattle, for it it easily conceivable that a human being having become infected from cattle may pass the infection on to other human beings. The dangers from bovine tuberculosis to man are sufficiently great to warrant strict precautions against it.

Infusoria in the Stomach.—Cohnheim (*Deut. med. Woch.*, 1909, xxxv, 92) refers again to the occurrence of infusoria in the stomach and œsophagus and reports seven new cases. The parasites live only in the absence of free hydrochloric acid, and thus far they have been found in the great majority of cases in patients with carcinoma of the stomach or œsophagus. They are most often found in the mucus or the muco-

purulent material. Trichomonads are most frequently present (megastoma has been found occasionally). Cohnheim has looked for the parasites in many cases of achylia gastrica which were not carcinomatous, and found them in only one case. In achylia associated with cancer in parts of the body other than the stomach he has failed to demonstrate the organisms. Of the cancer cases it is especially those that are ulcerative that are apt to show infusoria. Cohnheim does not believe the infusoria, especially the trichomonads, cause an enteritis. In all cases in which he has found them in the feces he believes they have been secondary to gastric disease.

Fat-splitting Ferment in the Lymphocytes.—BERGEL (*Münch. med. Woch.*, 1909, lvi, 64) has studied the ferments of the lymphocytes, especially with reference to fat-splitting ferment. The lymphocytes were obtained from (1) tuberculous pus; (2) the exudate resulting from subcutaneous injection of 1 to 2 c.c. of old tuberculin in guinea-pigs; (3) the spleen; and (4) lymph glands. He tried various substances, but found that plates of yellow wax and of neutral butter fat were the most satisfactory. On the yellow wax plates these substances containing lymphocytes caused crater-like depressions after being placed in an incubator at 52° for twenty-four hours. As controls, physiological salt solution, rabbit's serum, red blood cells suspension, tuberculin, lecithin, fibrin, amylum, and trypsin were used and produced no cupping. Human blood containing both lymphocytes and fat splitting ferment caused a slight depression on the surface of the wax. In a case of "mixed-celled leukemia, lymphocytes predominating," a well-marked cupping resulted. Tuberculous pus usually produced the greatest depressions. Neutral butter fat was rendered acid by the same substances, the control remaining neutral.

The Differential Diagnosis of Acute Leukemias.—SCHULTZE (*Münch. med. Woch.*, 1909, lvi, 167) refers to the difficulty that exists in differentiating acute lymphoid and myeloid leukemias. In the chronic cases the differential diagnosis is easy, but acute cases are quite the reverse, for here one has to differentiate the lymphoblast, the antecedent of the lymphocytes, from the myeloblast, which is the parent cell of the granular leukocytes. The two cells are practically identical in size, each possesses strongly basophilic protoplasm, and their nuclei are similar. Schridde describes a narrow clear border about the nucleus of the lymphoblast, but for most observers this is not a practical differential point. Schultze makes use of the so-called oxydase reaction (indophenoblausynthese) for differentiating these cells and especially for differentiating the tissues of lymphoid from those of myeloid leukemia. For carrying out this reaction a 1 per cent. aqueous solution of α-naphthol and 1 per cent. aqueous solution of dimethylparaphenylendiamin (E. Merck) are needed. The naphthol, which is only slightly soluble, is warmed and then filtered after cooling. The two solutions when united form a blue color under the action of light through an oxidative synthesis. In the presence of an oxidative ferment the process is greatly accelerated. Myeloid tissue when treated with these solutions is stained blue, owing to the presence of an oxidative ferment, while lymphoid tissue remains unstained. The method is especially applicable to tissue.

Pneumococcic Influenza.—CURSCHMANN (*Münch. med. Woch.*, 1909, lvi, 377) reports a series of cases admitted to his clinic in Leipzig during the fall, winter, and spring of 1907 and 1908 which were clinically typical cases of influenza. In 49 of these patients careful bacteriological studies were made of the sputum, and in none of them was Pfeiffer's bacillus found, although it had been practically constant in previous epidemics. In 46 of the cases there was found the Fraenkel-Weichselbaum diplococcus, which was characteristic in all respects, that is, capsule formation, extracellular occurrence, reaction to dyes, culture media, etc. In a large number of the cases this organism was present in the sputum in almost pure culture. In the remainder it was constantly found to be the predominating organism, so that there can be scarcely any doubt as to its etiological importance. In 20 cases mice were inoculated, with the characteristic results and autopsy findings. Curschmann feels justified in saying that the epidemic in Leipzig which was influenza clinically was due not to Bacillus influenzæ, but to Fraenkel's diplococcus. This finding in no way changes the status of the Pfeiffer bacillus, which wrought such havoc during the pandemic of 1889 to 1893.

SURGERY.

UNDER THE CHARGE OF

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The Surgical Treatment of Cancer of the Mouth.—STEINER (*Deut. Zeit. f. Chir.*, 1909, xcviii, 1) reports a study of 132 cancers of the mouth, including the tongue. These cancers rapidly extend locally and involve the neighboring lymph glands, because of the rich lymphatic supply. They may occur at any age from the second decade on: 57 per cent. of the 61 cancers of the cheek developed between the ages of forty-one and fifty-five years; 60 per cent. of the 51 cancers of the tongue and sublingual region between forty and sixty years; 3 per cent. of the whole 132 cases occurred in females. Congenital anomalies, scars, psoriasis, and leukoplakia, in many cases, preceded the cancerous formation. The free use of tobacco, by smoking and chewing, favors the development of cancer. Metastasis was shown in the neighboring lymph glands in the earliest stages of the growth. More remote metastasis is rare. The operation in every case should consist in the removal of the primary growth and the cleaning out by dissection of the cervical region on both sides. The operative mortality of cancer of the mouth was 24.1 per cent. It was least (4.5 per cent.) in cancers of the cheek, and greatest in those of the tongue. A radical cure, that is, with no

recurrence for more than three years, was obtained in 10.3 per cent. of the cases.

The Surgical Treatment of Cancer of the Breast.—STEINER (*Deut. Zeit. f. Chir.*, 1909, xcviii, 21) studied 170 cases of cancer of the breast. It is most frequent between the ages of forty and sixty years. Predisposing causes are heredity (3 per cent.), chronic inflammation (6.6 per cent.), trauma (17 per cent.), congenital anomalies, and Paget's disease. 2.6 per cent. of the cases occurred in the male breast. One mammary gland is no more disposed to become cancerous than the other. In half of the cases operated on by the Heidenhain method, the cancer had existed more than a year. The axillary glands were invaded in 65 per cent. of these, and in 35 per cent. the cancer was ulcerating. Ten per cent. of the primary cancers operated on by this method were free of recurrence more than five years after operation. In 53 of the 72 cases operated on by the more complete Halsted-Kocher operation, the cancer had been present more than one year before operation. Regional involvement of the lymph glands existed in 74 per cent. of the cases, and ulceration of the growth in 17 per cent; 27 per cent. of the cases operated on for primary growths were free of recurrence more than one year after operation; 21 per cent. of the cases operated on for recurrent cancers, remained free of recurrence more than five years after operation. In half of the cases which recurred, death occurred in the first year after operation, and always within the critical three years.

Snapping Hip Joint.—ZUR VERTH (*Deut. Zeit. f. Chir.*, 1909, xcvii) says that voluntary snapping of the hip is due to the ability, through contraction of certain muscles and the exclusion of others, to cause part of the fibers of the iliotibial band of the fascia lata to pass quickly over the great trochanter. This ability is inborn in many people, while most others can learn it. No troublesome conditions are associated with the voluntary type of snapping hip. Accessory diseases, like bursitis, can, of course, produce pain. It is not an infirmity, but a trick. The habitual snapping of the hip is a pathological condition, dependent upon inflammation of the fascia lata and its associated bursæ or upon paralyses, lacerations, or other chronic inflammations of the fascia or a part of the gluteus maximus. This condition expresses itself by certain involuntary audible and palpable quick movements over the great trochanter. It is associated with acute pain, and requires, according to its cause, operative or functional treatment. The changes in the relation of the trochanter to the pelvis after luxation of the fascia, can be so considerable that a careful examination by the eyes and palpation and a skiagraph will be necessary in order that it may not be mistaken for a dislocation of the femur. The diagnosis of a luxation or a subluxation of the femur must depend upon the proof that the head is entirely or partly outside of the acetabulum.

Double Nephrectomy and Re-implantation of one Kidney.—CARREL (*Archiv f. klin. Chir.*, 1909, lxxxviii, 379) has shown that a kidney extirpated and then re-inserted in place is in a condition to functionate so that the animal affected may live more than eight months. The technique of the operation of transplantation is so well developed that

it involves little danger in itself. Only one of six animals operated on died as a result of the operation. The four other deaths were the result of complications, such as tuberculosis, ascending pyelitis, and hydronephrosis, all of which can be avoided. Usually the animal recovers very quickly after the operation and conducts itself as before. A serious vessel or kidney complication, therefore, does not exist. After some weeks, the cicatrix at the line of union in the vessel wall is linear and does not induce secondary abnormal conditions, such as aneurysm, hemorrhage, or stricture. It is worthy of note that a kidney whose circulation had been stopped for almost an hour, and which had been kept in Locke's solution, and its nerves severed, should, after re-implantation, functionate in a normal manner and after eight months show no signs of disease. According to Bindo de Vecchio, division of the kidney nerves, causes symptoms of disease of the epithelial cells. The classical, physiological view is that enervation of the kidney leads to disturbance in the secretion of the urine. The quantity is abundant, the specific gravity diminished, and it contains albumin and red blood cells. In a dog, Carrel removed the right kidney and brought out the left kidney, which was left attached to the rest of the body only by the bloodvessels and ureter, the latter being as freely exposed as possible. Five days later the animal urinated 130 c.c. in twenty-four hours. After one month, 90 to 124 c.c. of urine was voided daily. This urine was of moderate density and contained no albumin. More than a year after operation the animal was still living and in good health. Carrel concludes, from his series of experiments in kidney transplantation and re-implantation, that the technique of the operation is sufficiently perfected to permit the avoidance of immediate or late complications arising from the bloodvessels. The ability to withstand the operation, the temporary interruption of the circulation, the washing of the kidney, and the division of the nerves is demonstrated by the excellent functional results in the organ more than eight months after operation.

Infection of Gunshot Wounds.—VON REYHER (*Archiv f. klin. Chir.*, 1909, lxxxviii, 576) says that a primarily infected gunshot wound may contain infecting material from the gun barrel, or the ball, shreds or fibers of clothing, or portions of epithelium. He concluded that every gunshot wound in war is primarily infected. Of the wounds from shrapnel-filled shells, 62 per cent. were infected, and of the wounds from jacketed bullets, 20 per cent. were infected. This would show that in 38 per cent. of the one and in 80 per cent. of the other type of wounds the organism is capable of mastering the infection by means of its own bactericidal strength. The secondary infections play a subordinate role in war. Primary infection is encouraged only in large caliber wounds, and is almost always associated with extensive wounds of the soft tissues. The most severe infections are primary. The severity of the wound controls in a measure the severity of the infection. The chief dangers of wounds come from the pieces of clothing carried in. These pieces are larger from shrapnel wounds than from the jacketed bullets. The clothing of soldiers in the field is very infectious. The number of severe infections was highest in the hospitals nearest the field of battle. The number of infections and the death rate decreased the further the hospital was from the battlefield.

Primitive Cancer of the Right Ureter.—ZIRONI (*Ann. des mal. des org. gén.-urin.*, 1909, i, 81) reports a case of cancer of the right ureter in a woman, aged thirty-six years. The kidney was exposed by operation and found hydronephrotic. By digital examination in the dilated ureter a mass was recognized in its wall and two small pieces excised. The kidney was fixed to the abdominal wall in the wound and gauze drainage introduced. Death occurred on the ninth day after operation. At autopsy the right ureter was opened, and it showed at its upper end three nodules, close together, and lower down several others. In the lower third of the ureter was found a mass about the size of a guinea-hen's egg in the wall of the ureter, in the centre of which was found a calculus about the size of a hazelnut. Sections from the different neoplasmic masses showed them to be cancers. Rokitanski and others have shown that the pavement epithelium which lines the pelvis of the kidney and the whole ureter may, as the result of simple calculus or tuberculous inflammation, be transformed into several layers, while the mucosa becomes infiltrated with round cells and consequently sclerotic. This condition is called leukoplasia and is frequently found on the tongue, the inner surface of the lips, or the vulva, and in the vagina.

Regional Anesthesia for the Transplantation of Skin.—NYSTROM (*Zentr. f. Chir.*, 1909, xxxvi, 137) says that in most of the cases in which he employs the Thiersch or Krause method of skin grafting, he produces regional anesthesia on the outer surface of the thigh by anesthetizing the trunk of the external cutaneous nerve through the skin, and then taking the skin grafts from the anesthetized area. The skin of the greater part of the outer side of the thigh is supplied by this nerve. A 1 per cent. novocaine solution is preferred, in which every 10 c.c. contains five drops of a 1 to 1000 adrenalin solution; 4 to 5 c.c. of this mixture is injected just to the inner side of and below the anterior superior iliac spine, and at varying depths, a part at least under the fascia lata, but not too deeply into the muscles. After ten minutes, which may be employed in cleansing the granulating surface to be grafted, the analgesia will be complete. When such preparation of the granulating surface is not necessary, the transplantation may be entirely painless, aside from the pricking of the hypodermic needle.

The Sensibility of Abdominal Organs.—KAST and MELTZER (*Mitt. a. den Grenzg. der Med. u. Chir.*, 1909, xc, 586), as the result of experimentation, reached the following conclusions: The abdominal organs in dogs, manipulated through a small opening in the abdominal wall, are evidently acutely painful. Inflammation increases markedly the pain in the abdominal organs of dogs. When all the intestines or a large part of them are drawn out or freely exposed, there is a marked decrease in sensation, which is the more marked the weaker the animal becomes. Simultaneously the animal becomes more apathetic and the sensitiveness of the skin is decreased. Laparotomy also depresses the motor activity of the gastro-intestinal canal. The motor and sensory depression depends upon a reflex inhibition which is central in origin and can extend to other centres. In weak animals and after a prolonged procedure the sensory inhibition extends to the vital centres in the medulla oblongata, and often leads to fatal shock. It appears also that

the peripheral mechanism in the intestinal canal is inhibited up to a certain point. The intestines of cats and small dogs also possess acutely sensitive nerves. They become exhausted easily, however, and by laparotomy are very quickly and strongly influenced. The nerves of the intestines suffer much more strongly and quickly than those of the mesentery. Surgical operations in men do not permit one to prove that the intestines in the normal closed body do not possess sensory fibers. Until more definite proof is offered that the sensory innervation of the human intestines differs radically from that of other mammalia, it must be accepted that, as in animals so in men, the abdominal organs are supplied with their own sensory nerves, and that the sensitiveness of these organs can be increased by inflammation, as in animals. This hypothesis explains in a simple manner the well-known occurrence of all kinds of severe pain in the human abdomen.

Experimental Investigations Concerning the Heart and Trauma.—Külbs (*Mitt. a. den Grenzgeb. der Med. u. Chir.*, 1909, xc, 678) says that valvular disease of the heart can result from trauma, indirectly, through violence applied to the chest wall. Pure lacerations of the valves have been found in such cases at autopsy, also bloody infiltration of the valves. That such injured and changed valves may become the seat of infection has also been shown, and a similar condition has been produced experimentally. When no infection takes place in such cases, there may develop under certain circumstances a gradual valvular insufficiency. Külbs was able, with relatively mild, blunt force applied to the chest wall, to produce in animals, frequently, extensive heart injuries without any considerable damage to the skin or chest wall. These injuries consisted chiefly in hemorrhages, most frequently in hemorrhages of the valves. Hemorrhages of the heart muscle and of the pericardium were produced also. The valvular hemorrhages, apparently, were mostly absorbed. The muscle hemorrhages were replaced by connective tissue. Judging from the frequent extensive hemorrhages at the bases of the valves extending deeply into the muscle substance, it is concluded that they do not heal without defects. In those cases in which gross anatomical defects were found postmortem, Külbs had not been able to detect previously, by auscultation or by the pulse, signs of cardiac insufficiency. In the causation of these lesions the yielding nature of the chest wall played an important part, as was shown by the varying experiments.

The Intra-abdominal Administration of Oxygen.—Bainbridge (*Annals of Surgery*, 1909, xlix, 305) had reported in a previous paper that he had employed oxygen by inhalation; by infusion into the pleural cavity; by injection into abscess cavities, carbuncles, furuncles, and other inflammations, acute and chronic; by injection into tuberculous joints; by infusion into the abdominal cavity, allowing the gas to be absorbed —in the following conditions: tuberculous peritonitis, with ascites; after removal of ascitic fluid from whatever cause; following severe laparotomies for the control of shock, for its influence upon hemorrhage, cyanosis, nausea, and vomiting, and for the prevention of adhesions. Since the publication of the paper referred to above, he has continued to test the utility of the intra-abdominal administration of oxygen whenever it seemed to be indicated. In this research the field of usefulness has

gradually enlarged. It is now administered to lessen shock, hemorrhage, nausea, and vomiting; to overcome negative intra-abdominal pressure after the removal of large tumors; to prevent the formation of adhesions; for its effect upon pus-producing organisms and their toxins. The gas is warmed, usually to a temperature of 90° to 100°, by passing it through a tube from the tank in which it is compressed into a wash bottle filled with hot water. This long exit tube is again connected with a piece of glass tubing, and to this, in turn, is attached a piece of sterile rubber tubing, through which the gas is introduced into the abdominal cavity. In this last piece of tubing, at the distal extremity, are two openings, one in the end which is cut obliquely, and the other in the wall of the tube near the end. When the gas is introduced the wound is first closed around the tube, and when the desired quantity is in the abdomen, a purse-string suture of the peritoneum is tied as the tube is carefully withdrawn. The abdomen is ballooned with the gas, which is gradually absorbed by the tissues. Bainbridge concludes from this study that oxygen, intra-abdominally administered, has a distinct field of usefulness in lessening shock, hemorrhage, nausea, and vomiting; in overcoming negative intra-abdominal pressure after the removal of large tumors; in preventing the formation of adhesions, or, when broken up, lessening the liabitity of their return; and in influencing favorably certain types of tuberculous peritonitis. In three cases, in which the gas was introduced into the peritoneal cavity in septic peritonitis, sufficient beneficial effect was noted to warrant the hope that further clinical experience may establish the efficacy of the gas as an adjuvant in the treatment of this condition.

The Value of the Leukocyte and Differential Counts in Appendicitis.—Pease (*Annals of Surgery*, 1909, xlix, 385) reports a study of 300 appendicitis cases treated in the Presbyterian Hospital of New York, in which leukocyte and differential counts had been made previous to, and the pathological lesions demonstrated at, operation. The more severe the pathological lesion the higher the leukocyte count and the higher the percentage of polymorphonuclear cells in the differential count. A good many of the cases of general peritonitis, however, gave a low leukocyte count, and thus reduced the general average below that of the average for abscess cases. The explanation is probably to be found in the overwhelming dose of infection which reduced the body reaction. It is impossible, therefore, to decide the pathological lesion present from the leukocyte count alone. The pathological lesion can be judged much more accurately from the differential count than from the leukocyte count. A polymorphonuclear count of between 85 and 90 per cent. indicates the presence of a severe process; above 90 per cent., a dangerous condition probably complicated by peritonitis; below 80 per cent., safety for the time being; between 80 and 85 per cent., a doubt. These rules held good for about four-fifths of the cases, there being many exceptions to each rule. One point, and probably the most important that this investigation has taught Pease, is that it is impossible to decide from the blood count alone what pathological lesion we shall find, or even to determine whether the case is severe or not. There are many exceptions and these we must learn to interpret by other means at our command.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Treatment of Pellagra.—BABES, VASILIN, and GHEORGHUS (*Berl. klin. Woch.*, 1909, xlvi, 237) refer to a previous report on the use of atoxyl in 65 cases of pellagra, of which 35 were cured, while the remainder were improved, with the exception of six patients with chronic mental trouble and grave complicating disorders. Following the publication by Loeffler of the successful treatment of trypanosomiasis in guinea-pigs by a combination of atoxyl injections with internal and external applications of arsenic, they resolved to try this therapy in pellagra. Their patients were treated in the following manner. They were given an injection of atoxyl, 0.5, at the same time 1 to 5 mg. of arsenous acid in pills and an inunction of 5 grams of a salve, containing arsenous acid in proportion of 1 to 50. Mild cases received a single combined treatment as above. In other cases this was repeated on the succeeding day. In severe cases the treatment was repeated after an interval of a week on two successive days. This method of treatment was applied in 14 cases of pellagra, and was attended with remarkable results. Within one to four weeks complete cure resulted in every case. None of the cases required more than four applications of the combined treatment. The cures included both acute and chronic cases, some of the latter having suffered for as much as twenty years. All symptoms seemed to be equally favorably influenced; that is, erythema, œdema, mental symptoms, diarrhœa, etc. It is too soon to speak of a permanent cure, but the results obtained were very striking.

The Treatment of Sciatica by deep Perineural Infiltrations of Salt Solution.—HECHT (*Jour. Amer. Med. Assoc.*, 1909, lii, 444) reviews the results of deep intraneural and perineural injections of various solutions in the treatment of sciatica. He includes his personal observations in sixteen cases of sciatica treated by injections of alcohol, normal salt solution at body temperature, normal salt solution refrigerated to zero centigrade, and β-eucaine salt solution. His conclusions as to the proper technique and the best solutions are based upon the conclusions of many different observers less than upon his own personal observations. He condemns the injection of alcohol in sciatica because of the danger of subsequent motor paralysis. This is accounted for by the fact that the sciatic nerve contains both motor and sensory filaments and its fibers are essentially terminal. The results have been less dangerous in treating the trigeminal nerve, because, though containing motor fibers, it has rich anastomoses with the seventh nerve and the filaments of the different branches anastomose with each other, and the nerve is therefore capable of some regeneration if degenerative changes occur. He

quotes the results of various observers, as follows: Schloesser reported thirty-six cases of sciatica treated by alcohol injections, with thirty-six cures. Erb, of Heidelberg, Fischler, Brissaud, Levy, and Baudoin, of Paris, tried injections of alcohol, with many negative and not a few disastrous results. Experiments on animals have shown that alcohol exerts a markedly destructive action upon the medullary sheath and axis cylinder of the nerves so treated, but that cocaine and salt solution did not have this effect. Lange was the first to inject normal salt solution at body temperature, using large quantities, 80 to 120 c.c. Lange also made use of β-eucaine salt solution at body temperature injected in amounts of from 60 to 100 c.c. He treated 56 cases in all, of which 65 per cent. were completely cured, 10 per cent. were improved, and 10 per cent. had a recurrence. In 15 per cent. of his cases the result was a total failure. Schlesinger used normal salt solution refrigerated to zero centigrade in smaller quantities, 10 to 20 c.c. He treated 42 cases with excellent results. Busse has treated 81 patients who had sciatica with injections of an 0.8 per cent. salt solution, and records 63 per cent. complete cures and 21 per cent. improvements. A number of other observers give correspondingly good reports. Hecht prefers the use of normal salt solution of varying temperature and quantity, or the beta-eucaine solution of Lange for the injection. He advises the injection of the sciatic at its point of exit from the great sacrosciatic foramen. Several methods are in use for the determination of this point. Hecht found that he could invariably locate it in the following manner: The patient should lie on the abdomen with fully extended legs and a flat pad placed in the hollow of the groin. A line is drawn with tincture of iodine from the sacrococcygeal articulation to the postero-external border of the great trochanter; at the junction of the inner one-third with the outer two-thirds of this line is the spine of the ischium. Placing the needle a thumb's breadth to the outer side of this point and penetrating in a directly perpendicular line to a variable depth, one engages the sciatic nerve. He uses an all metal syringe of 60 c.c. capacity. The needle is steel, 12 cm. long, with a caliber of 1.5 mm. and provided with a half sharp point which is protected by a dull tipped stylet. The needle fits to the syringe by a slip-tip. The needle with the stylet partly withdrawn is put through the skin, and when well in the subcutaneous tissue the stylet is returned to cover the point and the needle is directed perpendicularly to the necessary depth. The moment the nerve is touched the patient feels a sharp lancinating pain at the heel or in the calf associated with a quick jerky movement. Occasionally the pain is felt in the buttock, thigh, or at the knee. The filled syringe is now attached and the solution injected slowly with steady, firm pressure. Considerable soreness may exist for a while at the point of injection, but this soon passes away. Hecht had no serious accidents or complications. Immediate relief is afforded by the first injection, though several injections may be necessary to effect a cure. He says that a large number of the cases have been followed for from one to four years, and many patients have been entirely free from pain, while under observation. His review of the treatment led him to believe that improvement commonly occurs, that recurrences are not the rule, and that failures are the exception.

Calcium Chloride as Preventive for Serum Sickness.—GEWIN (*Münch. med. Woch.*, 1908, li, 2670) gave every alternate patient in a series of 200, calcium chloride by the mouth when diphtheria antitoxin was injected. He found that in those patients receiving the calcium chloride there was either no disturbance at all or at the most very slight. He gave 1 gram (15 grains) with the larger doses of serum and 0.5 gram with the smaller doses.

The Röntgen Ray Treatment of Blood Diseases.—ELISCHER and ENGEL (*Ztschr. f. klin. Med.*, 1909, i to iii, 31) report 44 cases of leukemia, lymphosarcoma, or mediastinal tumors treated by the Röntgen rays since 1904. They include in this report the detailed histories. They believe that it is most important to apply the treatment in the early stages. When applied later the rays must be more intense and consequently there is much more danger. In the early stages of cervical glandular processes and mediastinal tumors there need be no fear of destroying large masses of tissue with the consequent intoxication. They advise the use of the rays in all cases of enlarged cervical glands because of the difficulty in the early differentiation of a simple or tuberculous adenitis from a lymphosarcoma or a pseudoleukemia. They advise strong daily exposures of eight or ten minutes for from ten to fourteen days. The exposures are then suspended in order to determine the patient's sensitiveness to the rays. After a period of observation the treatment is resumed until signs of improvement appear. In a few cases the rays will be found without value. If good results are not obtained with ten minute exposures, the treatment must be stopped, since a longer exposure would inevitably result in a burn. The exposures are kept up two or three months in the case of a mediastinal tumor. They say that the early treatment is of even greater importance in leukemia. Shorter exposures must be made with great caution to avoid injuring the capsules of the spleen and to prevent toxic symptoms. The main point in leukemia is to work with as small a dosage of the rays as is possible, utilizing the late action of the rays. After eight or ten exposures the treatment is suspended for a week. With careful watching of the patient's blood and weight, and a renewal of the treatment whenever the least sign or symptom of a recurrence occurs, they believe that the fatal outcome may be long postponed. They think that an acute exacerbation is more liable to occur in the cases treated by radiotherapy. In one case six courses of treatment were given during three and one-half years, always with marked benefit, but no authentic case is on record of actual permanent recovery. The tissues seem gradually to acquire an immunity to the action of the rays, which then become useless. Of the 19 cases of leukemia treated, 10 of the 13 myeloid type and 2 of the 6 lymphatic variety were much improved by the treatment. The prognosis of the result of the radiotherapy cannot be accurately made in many cases. The prognosis does not especially depend upon the length or the severity of the disease. In general, acute cases and chronic cases with acute symptoms, such as fever and a rapid loss of weight, derive little benefit from the treatment. A review of the literature shows that radiotherapy has a favorable influence in 90 per cent. of the myeloid type and in 65 to 70 per cent. of the lymphatic variety.

The Influence of Certain Drugs upon Peptic Digestion.—ASCHER (*Archiv f. Verdauungskrank.*, 1908, vi, 629) has performed some experiments with a number of drugs in order to determine their action upon pepsin digestion. He used Jacobi's ricin test as a measure of the amount of proteid digestion in test-tube experiments. He found that solutions of sodium chloride, sodium sulphate, and potassium iodide had no effect unless in concentrated solution. On the other hand, alcohol, sodium salicylate, different preparations of iron and arsenic, all inhibited more or less completely peptic digestion. Iron especially had a marked inhibitory action. Of the preparations of arsenic, atoxyl and sodium cacodylate had less of this action. He also determined that lactic and acetic acids did not affect the digestion of proteid in the presence of decinormal HCl unless in considerable concentration. The use of decinormal lactic or acetic acids in place of decinormal hydrochloric acid in the test-tubes caused very little digestion of proteid. His experiments showed that small quantities of tannin and of the bitters, quinine and condurango, markedly inhibited the action of the peptic ferment.

Changes in the Size of the Heart Induced by Hot and Cold Baths.—BECK and DOHAN (*Münch. med. Woch.*, 1909, iv, 171) made a series of observations regarding the influence of hot and cold baths upon the size of the heart. An orthodiagram of the heart was taken before the baths, a second one directly after, and in some of the cases a third was taken twenty to sixty minutes after the bath. They found that after the hot baths (104° to 106° Fahrenheit) there was a considerable diminution in the apparent size of the heart in six of the seven cases. There was no apparent change in the seventh case. After cold baths (68° to 77° Fahrenheit) they found in four of the five cases an increase in the size of the heart. Three showed a very considerable increase. They also noted that the hot baths increased the pulse rate and lowered the blood pressure, while the cold baths did the reverse. Some think that this is explained by a reflex action on the vagus and accelerator nerves, hot baths stimulating the accelerator and inhibiting the vagus, and cold baths vice versa. They think that probably the important action is an altered distribution of the blood in the body.

The Treatment of Acute Articular Rheumatism.—PLEHN (*Deut. med. Woch.*, 1908, li, 2201) says that the success of the salicylate treatment of acute articular rheumatism depends on sufficient dosage. When so given, he thinks the action of salicylic acid is as specific as the action of quinine in malaria or of mercury in syphilis. He gives 1 gram every two hours, so that the patient takes 6 grams a day, suspending the medication at night. This is continued until the temperature has been normal for three days and all joint symptoms have disappeared. He then gives 4 grams a day for a week. Three further days in bed without drugs are insisted upon before the patient is allowed to get up. The painful joints are dressed with dry cotton and supported on cushions. This method is applied to every case, no matter how mild it may seem, and he regards it as the minimum dosage necessary for the proper treatment. Women, as a rule, do not tolerate such large doses, and he consequently reduces the dosage to 5 or even 3 grams a day. As a rule, the dosage should correspond to 0.08 gram per kilogram of body weight.

In 319 cases so treated, with the heart normal, valvular trouble developed in only two cases, and in these this method had not been carried out strictly. In 101 cases of recurring rheumatism, in which the first attack had been treated elsewhere, heart trouble developed in 36 cases. Plehn is convinced that this method of early, vigorous, and long-continued salicylate treatment saves the patient from complications on the part of the heart and pleura. He believes that salicylic acid in doses of 8 grams a day, continued for long periods of time, has no toxic effect upon the heart. It can be given without bad results in chronic valvular disease and myocarditis. He says that existing acute or chronic nephritis was always favorably influenced by this treatment. He believes that baths and packs reinforce the action of the drugs, but never take their place. He suggests for the rare cases which resist the salicylate treatment either the intramuscular injection of quinine with antipyrin or the intravenous injection of colloidal silver.

The Effective Treatment of Acute and Subacute Rheumatism.—Lees (*Brit. Med. Jour.*, 1909, i, 146) believes that rheumatic fever is a specific infectious disease, the manifestations of which differ widely in children and in adults. He believes that in childhood the heart is always affected to a greater or less degree, but that the joints may only be slightly and often not at all affected. When it attacks adults, the most prominent manifestation is an arthritis. He attributes to the salicylates a specific action against the rheumatic microbe or poison. For this purpose the salicylates must be given in sufficiently large doses. He believes that practitioners are satisfied ordinarily with the cure of the more easily controlled manifestations—the arthritis and the pyrexia. He deprecates this attitude and speaks for the more energetic use of the salicylates to ward off cardiac complications. The addition of double the amount of sodium bicarbonate to each dose of the salicylate will help to prevent the unpleasant symptoms which may prevent the use of a sufficient amount of sodium salicylate. The initial dose for an adult should be 15 grains given every two hours from 6 A.M. to 10 P.M., or 150 grains daily. A child aged from seven to twelve years should receive 10 grains every two hours, or 100 grains daily; for a child younger than seven, 5 grains at a single dose, or 50 grains a day. The amount of the daily dosage should be increased each day, or every second day, until unpleasant symptoms are produced. These are deafness, tinnitus, vertigo, vomiting, etc. Drowsiness in children, an acetone odor to the breath, or acetonuria, with slowing and deepening of the respirations, are danger symptoms. He points out that these symptoms may be entirely prevented by the relief of constipation and the use of sufficient sodium bicarbonate. The daily increase of the dosage may be from two to 5 grains in the individual dose. The amount needed for a child may be nearly as great as for an adult, for in a child the infection is more virulent and more often affects the endocardium. In a child, also, the drug is eliminated more quickly in the urine. In mildly acute and subacute cases a daily dose of 150 grains may be sufficient, but in many it is necessary to increase this to 200 and 250 grains a day, and in some severe cases to 350 and 400 grains. Chorea may require 250 to 400 grains daily.

PEDIATRICS.

UNDER THE CHARGE OF
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Report of Ten Cases of Epidemic Cerebrospinal Meningitis Treated with the Antimeningitis Serum.—J. D. MORGAN and W. W. WILKINSON (*Arch. Int. Med.*, 1908, ii, 256) report their experience with 10 cases of epidemic cerebrospinal meningitis treated with antimeningitis serum; 7 of these were in children and adolescents; 7 (5 children) of the patients recovered, and 3 (2 children) died, giving a mortality percentage of 30; one of the deaths was in a case of chronic hydrocephalus, and, omitting this patient, the mortality percentage is 22. Following the serum injection there was usually considerable improvement in the clinical symptoms. The course of the disease was considerably modified, an average of twenty-three days for all 7, and in 5 of the cases fifteen days. Only 2 of the patients, who recovered, suffered from sequels. The serum caused a marked diminution in the number of diplococci in the spinal fluid, a disappearance or degeneration of the organism in coverslips, and in the majority of cases its growth was promptly inhibited. Phagocytosis was either unchanged or increased. In 5 out of 8 cases the leukocytes showed degenerative changes following the serum injection. This explains the rapid clearing of the spinal fluid observed following the injection. The leukocyte count rose in 3 cases, in all of which the patient recovered. It fell in 5 cases, in 2 of which the patients died.

Blood Examinations in Nurslings Afflicted with Hereditary Syphilis.—H. RISEL (*Münch. med. Woch.*, 1908, lv, 2160) publishes the results of 51 blood examinations of 20 infants known to have hereditary syphilis. Of these children, one was less than one month old, 6 were in their second month, 8 in their third month, 4 in their second quarter, while one was almost one year old. In all of them the hemoglobin was reduced; the same was true of the red corpuscles. In lighter cases their number averaged about 3,000,000; in graver cases it fell to as low a point as 1,500,000. In such cases other disturbances of red corpuscles were also noted, such as variations in the size of the cells, poikilocytosis, basophilia, and in very grave cases also basophilic granulation. Nucleated red corpuscles were found in all cases with the exception of the very lightest ones; in graver cases microblasts and normoblasts with pyknotic nuclei appeared in the blood, while in the gravest types there were normoblasts with radial nuclei and megaloblasts. In even the lighter cases the erythroblasts amounted to about 5 per cent. of all the nucleated cells, while in one instance they amounted to even 27 per cent. In only 14 of the cases was a marked leukocytosis (over 20,000) observed, thus showing leukocytosis to be relatively rare. It is usually associated with the appearance of septic complications or bronchopneumonia. In most of the cases the leukocytoses are of a

polynuclear neutrophilic character. In favorable cases there may be also lymphocytosis with high leukocytic values, but it is much more frequent, particularly in grave cases, to find lymphocytosis with normal number of leukocytes. No definite explanation can be found for the basophilic and eosinophilic polynuclear leukocytes, but the mononuclears are always increased in grave cases. In most instances isolated myelocytes are found, the percentage varying from 0.5 to 5.6 per cent. in the grave cases; the greater the number the more unfavorable the prognosis. The myelocytes are of a neutrophilic and eosinophilic character. The myelocytic picture is usually accompanied with a large number of erythroblasts. The gravest blood changes were found in the youngest of the children. As all of these were breast-fed children, this can with right be attributed to the syphilitic infection. Clinically all these had enlarged livers and spleens, and a number of them presented pseudoparalyses of some or all of the extremities; 13 of the patients died.

The Influence of Phosphorus Cod-liver Oil on the Metabolism of Healthy and Rachitic Nurslings.—W. Birk (*Monats. f. Kinderheilk.*, 1908, vii, 450) bases his observations upon a study of four children between the ages of eight and ten and one-half months; two were in good health, the others were rachitic. First, the metabolic changes were noted for three days, the food given being the ordinary diet given such children at the Breslau children's clinic. They were then given from two to three times daily one-half to one teaspoonful of a phosphated cod-liver oil; a week later the influence of this medication on metabolism was noted over another period of three days. The results confirm the favorable results of this oil on rickets. The results of the experiments are thus tabulated: (1) It was determined that in some rachitic children the mineral excretion was greater than the amount of such salts taken up. (2) In such cases the phosphated oil produced an improvement, as judged by the increased retention of ash, calcium, and magnesium. The phosphorus metabolism was not markedly influenced by the phosphated cod-liver oil. (3) The organism was not found deficient from the standpoint of retaining function. (4) Neither was the amount of minerals taken deficient in amount; as soon as the phosphated oil was given, the retention increased even though the amount of mineral substances taken in was not increased. (5) The condition, therefore, must be the result of a pathological excretion of these salts. (6) The digestion of fats in the intestine was also favorably influenced by the oil; an antagonismal state exists between the formation of soap and retention of lime: as the lime retention increases, the soap formation decreases. (7) The favorable action of the phosphated oil must in some way be connected with this change in soap formation.

Lordotic Albuminuria.—H. Nothmann (*Archiv. f. Kinderheilk.*, 1909, xlix, 216) agrees with Jehle, who found that the so-called orthostatic albuminuria was not due so much to a change from the horizontal to a vertical position, but rather to a lordotic deformity of the spine. Nothmann observed that all cases of orthostatic albuminuria were in such individuals, and that lordotic albuminuria existed in patients

who had otherwise no symptoms or signs of kidney disease. He was able to produce such an albuminuria by placing patients, who ordinarily had no albuminuria, in a lordotic position while in bed, the albumin disappearing when the position was altered. He was able to increase the amount of albumin by placing patients with renal disease in a lordotic position, and he was able to reproduce it in patients in whom the albumin had disappeared altogether, simply by forcing such a position. A more marked degree of lordosis is necessary to produce an albuminuria in a healthy individual than in one with nephritis. From a series of observations of the albuminuria of scarlet fever patients he concludes that it is frequent, usually slight, generally lasts but a short time, but may return during the course of convalescence several times; there may or may not be an organic sediment; it may appear with the patient lying quietly in bed or after he rises; it may be associated with other sequels or may be the only remaining injury of the disease. In all convalescents, however, the same albuminuria and acetic acid precipitate could be produced by inducing a lordosis, and in no patient in whom the lordotic experiment was negative were there ever symptoms of a pathological or functional kidney disturbance noted. The cause of the albuminous excretion after scarlet fever is more of a functional than pathological nature. The anatomical change is probably a slight "catarrh of the uriniferous tubules." The disease is benign and disappears usually in a few days to weeks, the patient resting quietly in bed.

OBSTETRICS.

UNDER THE CHARGE OF

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The Treatment of Placenta Prævia.—SELLHEIM (*Monats. f. Geb. u. Gyn.*, 1909, xxix, 1) writes an open letter to Professor Martin urging the claims of extraperitoneal suprasymphyseal Cesarean section in the treatment of placenta prævia. Sellheim urges that the tedious uncertain methods of vaginal dilatation, with their mortality and morbidity, should be abandoned in placenta prævia in favor of modern surgical operations. He urges as a reason for this the great improvement in mortality and morbidity and the more prompt and lasting convalescence of the mother. The method of Cesarean delivery which Sellheim urges consists in opening the abdominal wall just above the pubes, taking care to avoid the peritoneum; the emptied urinary bladder is carried strongly downward or else above the brim of the pelvis, while the peritoneal sac is pushed upward; the operator thus seeks to avoid opening the peritoneal cavity. The lower uterine cervix, and, if necessary, the cervix, is incised sufficiently to deliver the child. If there is sufficient dilatation, the placenta may be expressed through the vagina, or, if such is not the case, it is manually removed. Should there be a tendency to

hemorrhage, the uterus is tamponed with iodoform gauze, which is subsequently removed through the vagina. If the case is septic the wound may be left open, the edges of the uterine wound being sutured to the margins of the abdominal wound. The uterus may then be drained with gauze. A uterine fistula is thus established, which is allowed to close spontaneously as the patient recovers.

The Toxicoses of Pregnancy.—FELLNER (*Monatschr. f. Geb. u. Gyn.*, 1909, xxix, 1) calls attention to the disturbances in the secretory nerves occasioned by pregnancy. Should toxemia develop, the nervous system becomes greatly disturbed. Fellner has endeavored to ascertain the exact factor in eclampsia which produces these psychic developments. He believes that the placenta plays an important part, because in several cases he has observed a cessation of the psychosis following the removal of retained placental tissue. He believes that an exaggeration of physiological processes, rather than the development of an entirely new pathological condition, causes these conditions. He draws attention to some of the phenomena of menstruation as similar to eclampsia and also the characteristic pain of osteomalacia.

The Management of Labor in Contracted Pelves is the title of an interesting book by BÜRGER, assistant in the first obstetric clinic in Vienna. This book, so far as we know, has not yet been translated into English. The material studied was 4240 cases of contracted pelves occurring among 49,375 patients, a percentage of 8.5. The book is written from Pinard's standpoint, but we may hope that obstetric science will reach that point where no child will be sacrificed in the interest of the mother. Contracted pelves are divided into four classes, the true conjugate of the fourth being 6.5 cm. Cases of atypical contraction are not considered, as each case must be considered upon its individual merits. Cases complicated by eclampsia, placenta prævia, or in which the child weighed less than four and one-half pounds, are also excluded. The general plan of treatment employed has been an expectant one. If the conjugata vera measured 8 cm., except in simple flat pelves, spontaneous labor was not expected. Symphysiotomy was performed for conjugata vera between 9 and 7 cm. The highest application of the forceps was always tentative and never forcible. The lowest forceps application was made only when danger threatened the mother or child. In breech cases the finger in the groin was the only method of making traction advisable.

The percentage of spontaneous deliveries was high. In primigravidæ with flat pelvis, when the true conjugate was between 8.5 cm. and 7.6 cm., there were 56.4 per cent. of spontaneous deliveries. With primigravidæ having generally contracted pelves, with the same true conjugate, there were 62.7 per cent. of spontaneous deliveries. When the true conjugate was from 7.5 to 6.5 cm., the percentage of spontaneous deliveries varied from 9.95 to 18. In general, varying with the degree of contraction, there were in all kinds of contracted pelves, from 89 to 9.9 per cent. of spontaneous deliveries. Bürger thinks that prophylactic version should seldom be performed. Premature labor was induced in only 0.6 per cent. of all cases of pelvic contraction, and 47 per cent. of the infants were lost.

Bürger believes that the induction of premature labor should be reserved for cases in which the patient has borne previously large and well-developed children, where some of the difficulties in delivery can undoubtedly be overcome by the mother. If the induction of labor is not followed by spontaneous delivery, vaginal delivery is rarely indicated, and in highly contracted pelves should never be attempted. Symphysiotomy is replaced by hebotomy. This operation was done twenty-three times, with no maternal mortality, and with the loss of one child. If both mother and child are to be saved, there is no question that Cesarean section is the preferable operation. Hebotomy is less dangerous for the mother, and in selected cases not much more dangerous for the child. Bürger believes that in the future premature labor and prophylactic version will very rarely be performed. Hebotomy will take the place of some cases in which Cesarean section is now performed.

GYNECOLOGY.

UNDER THE CHARGE OF

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The Ureters after the Radical Abdominal Operation for Carcinoma of the Uterus.—W. WEIBEL (*Zeitschr. f. Geb. u. Gyn.*, 1908, lxii, 184), as assistant to Wertheim, reports the occurrence of ureteral fistulæ in 24 out of 400 cases operated upon for carcinoma of the uterus. In 3 cases there was a fistula of each ureter. It is believed that the fistulæ in all cases arose from necrosis due to extensive dissection interfering with the blood supply of the uterus. Actual injury to the ureters during operation occurred 8 times in the first 200 and 3 times in the last 200 operations, and was in nearly every instance observed at the time and successfully remedied. The fistulæ appeared never earlier than the seventh nor later than the eighteenth day after operation, and were usually observed during the second week. Spontaneous healing occurred in 13 out of the 24 cases, beginning in one instance as early as the second week after the appearance of the fistula and taking place in another case as late as the fourth month. Usually spontaneous closure took place between the third and twelfth weeks; 2 of the 3 cases of bilateral fistula healed spontaneously. A nephrectomy was performed in 7 of the 11 cases in which spontaneous healing did not occur after long intervals, and is the operation recommended under such conditions. Cystoscopic examinations in cases of fistula followed by spontaneous healing showed in most cases a marked prolongation of the interval between contractions of the affected ureter as compared with the normal one, and in many cases a diminution in the intensity of the stream of urine. No other symptoms were observed in such patients.

Prolapse of the Rectum and Sigmoid Flexure following Hysterectomy.—L. J. HIRSCHMAN (*Jour. Amer. Med. Assoc.*, 1908, li, 1125) reported 2 cases in which such prolapse had occurred, and believes this result should be remembered in doing hysterectomy. Hirschman believes that when chronic constipation exists before hysterectomy the broad ligaments should be sutured together and proper treatment be addressed to injuries of the vaginal wall and perineum; that when any tendency to prolapse of the rectum or sigmoid is observed, mesosigmoidopexy should be done as a prophylactic measure, and that this operation should be the one of choice in every case of complete prolapse of the rectum and sigmoid, whether following hysterectomy or from other causes, as it holds the sigmoid in place by its natural support.

Intraligamentous Fibroids.—ERDMANN (*Amer. Jour. Obst.*, 1908, lviii, 861) says that he is convinced fibroid tumors developing within the broad ligament and independently of the uterus are by no means rare; the text-book descriptions of them are very meagre and the literature of the subject is very limited. Erdmann reports 4 cases in which he has operated removing the tumor and body of the uterus in each instance. Erdmann thinks the growths develop entirely from the broad ligament structures and that the differential diagnosis is based upon their usually slow growth, the elongation of the vagina, with a tumor, harder upon palpation than a cyst, with markedly limited mobility, more marked on one side of the pelvis, and the uterus, practically normal in size, tilted greatly to the unaffected side. Erdmann believes, however, that one cannot make a positive diagnosis before opening the abdomen, and refers to two chief dangers in their removal, hemorrhage from the iliac vessels or some of their branches and ureteral trauma.

Ureterovesical Anastomosis.—R. L. PAYNE (*Jour. Amer. Med. Assoc.*, 1908, li, 1321) reports 2 cases of this surgical procedure done by a method that is claimed as new. In 1 of them Payne loosened the corresponding kidney and depressed it to lessen the tension on the newly made junction of the bladder and the ureter. Payne does not mention whether in his 2 cases he avoided the misfortune of the formation of calculi about the portions of the sutures exposed to the urine, as has been recorded by many surgeons.

Early Rising after Laparotomies.—F. COHN (*Zentrlbl. f. Gyn.*, 1908, xxxii, 1233) comments on the results secured in 100 laparotomies in which the patients were allowed to get out of bed during the first week after operation, 13 arising on the first day, 16 on the second, 21 on the third, 30 on the fourth, 10 on the fifth, 8 on the sixth, and 2 on the seventh. Embolus was not observed. There were 3 cases of thrombosis, each of which was attributed to causes other than the early getting out of bed. One occurred in a woman, aged seventy years, from whom an immense ovarian cyst had been removed, and 2 in patients who had a moderate degree of fever previous to operation. The author advises caution in permitting the early getting up of patients who show before operation a rise in temperature or a disturbance in the circulation in the pelvis or lower extremities.

The Conservative Surgeon and the Symptomless Uterine Fibroid.—THOMAS B. EASTMEN (*Jour. Amer. Med. Assoc.*, 1908, li, 972) refers to the 12 per cent. of carcinomatous, sarcomatous, necrotic, and myxomatous degenerations as conditions, which if not removed will, at least, in all probability, terminate fatally, and if not removed such developments will occur as will render subsequent surgical procedure much more difficult and less productive of satisfactory results, as well as being conditions that in the majority of cases could exist unknown and even unsuspected by the examiner. Eastmen also refers to conservative surgeons removing benign growths from other parts of the body as well as the vermiform appendix after the subsidence of an inflammatory attack of that structure, and pleads for application of the same conservatism in the surgical treatment of uterine fibroids.

Ectopic Gestation with a Viable Child.—WERDER (*Amer. Jour. Obst.*, 1908, lviii, 796) advocates prompt abdominal section and total removal of the child and the placenta in cases of ectopic pregnancy with a viable child. Upon the fact that most of the blood supply to the placenta comes from the ovarian vessels and the uterines at the cornua of the uterus, Werder bases the plan of procedure he proposes, and which is as follows: After opening the abdomen, first secure the vessels in the infundibulopelvic ligament and then the vessels at the junction of the uterus and the Fallopian tube. If the pregnancy sac prevents exposure of these points, then compression of the aorta after delivery of the fœtus should be applied until the vessels mentioned can be secured, which is usually after considerable dissection. Then the fœtal sac and the entire placenta should be removed. For compressing the aorta Werder prefers Halstead's metal band or an ordinary broad clamp, the blades of which have been protected by rubber tubing, such as an intestinal clamp. This should not be tightened until after delivery of the child. The sac and placenta may then be removed leisurely.

Malignant Adenoma of the Cervix Uteri.—F. KLINGER (*Ztschr. f. Geb. u. Gyn.*, 1908, lxiii, 56) reports a case of adenoma of the cervix which developed so rapidly that in the course of four weeks from the first examination an operation was no longer considered advisable. He discusses the literature of this subject and concludes that instead of there being 20 cases on record, as estimated by Schidkowski, there are only 5 including the 1 here reported. He restricts the term to a malignant neoplasm in which the irregularly developed glands show only one epithelial layer.

The Anatomical, Physiological, and Pathological Relationship of the Uterus and the Stomach.—F. J. TAUSSIG (*Jour. Amer. Med. Assoc.*, 1908, li, 1005) states that if we exclude, first, the cases in which physical conditions in the abdomen through relaxed walls and pelvic floor have caused gastric and uterine symptoms; second, the cases in which the condition of the blood, as in anemic or chlorotic individuals, causes altered function on the part of both the stomach and the uterus; third, the cases in which there is hysteria, neurasthenia, or a general neurotic temperament; and finally, those of toxemia of various kinds, little is left to be called reflex neurosis. A few cases, doubtless, will be found

but these will be constantly lessened as pathology is better known and methods of diagnosis become more accurate. Taussig thinks that until a better understanding of the anatomy and physiology of the sympathetic nervous system is had, conservation in assertions regarding reflex neuroses of the stomach and uterus should be used and, more particularly regarding advocacy of operative intervention for the relief of such symptoms.

Metastases in the Central Nervous System and Organs of Special Sense from Carcinoma of the Uterus.—H. OFFERGELD (*Ztschr. f. Geb. u. Gyn.*, 1908, lxiii, 1) calls attention to the rare occurrence of metastases in the nervous system following primary carcinoma of the uterus, stating that only about 30 such cases have been reported. In a total of 6650 cases of uterine cancer reported by six authors this condition was found in only 3 instances. Metastatic growths from cancer of the uterus are much less frequent in the nervous system than in the liver and lungs, but more frequent than in the spleen, heart, adrenals, and thyroid gland. Metastatic carcinoma may develop in any part of the central and peripheral nervous system, including the meninges. Metastases in the brain, which may appear relatively early and even in cases deemed operable, are apt to be associated with secondary growths elsewhere, especially in the liver and lungs, and are all of hematogenous origin. They are usually solitary, rarely as large as a hen's egg, and usually give rise to no clinical symptoms. Metastases in the dura occur usually in inoperable cases, and are for the most part small but multiple, of lymphogenous origin, and give rise to no clinical symptoms. Metastases of the peripheral nerves occur in the pelvis, and are probably much more common than has been suspected. Only in very advanced cases has carcinoma of the uterus been known to give rise to metastases in the organs of special sense, and these are probably hematogenous in origin.

The Vesico-vaginal Interposition of the Uterus.—F. PETRI (*Ztschr. f. Geb. u. Gyn.*, 1908, lxiii, 559) calls attention to the frequent relapses (30 per cent.) following operations for prolapse of the uterus, appendages, and vagina when the operation was restricted to the vaginal wall and perineum, and describes his manner of performing Schauta's operation, in which the uterus is inverted and fastened between the vagina and bladder. He reports 14 cases. Of 11 of these, only 2 showed any relapse after six to twenty-one months and these were in old individuals in whom there was much atrophy of the uterus. Two died of intercurrent affections and one met with an accident soon after the operation, in which the uterus was torn loose from the vaginal wall and the bladder. In the latter instance a ventrofixation of the uterus was subsequently performed. Petri summarizes the results reported up to the present time by other operators following either Schauta's or Wertheim's method, or a combination of the two. Bucura had 1 relapse in 16 cases; Schauta, 1 severe and 2 slight relapses in 40 cases; Doederlein, 1 severe and 9 slight relapses in 44 cases; Krönig, 1 slight relapse in 15 cases; Fuchs, 1 relapse in 20 cases; and Scharpenak, 5 relapses in 45 cases subsequently examined.

The Vaginal, the Vertical Abdominal, and the Pfannenstiel Incisions.—E. E. MONTGOMERY (*Jour. Amer. Med. Assoc.*, 1908, li, 912) states the advantages and disadvantages of each of the incisions mentioned in the title of his paper. As advantages of the vaginal incision or route into the pouch of Douglas, Montgomery states: (1) That drainage is from the most dependent part of the peritoneal cavity. (2) In a fair proportion of cases it permits the cure of the patient by a less radical procedure. (3) The convalescence of the patient, even after hysterectomy, is more rapid and attended with less discomfort than is associated with the same procedure through the abdomen. (4) Ventral hernia and ventral adhesions are obviated. (5) In proper cases it permits the amputation stumps of the ligaments of the uterus to be brought outside the peritoneal cavity, thus facilitating the control of possible secondary hemorrhage. The disadvantages of this route are given as: (1) Insufficient exposure of the field of operation to sight. (2) Extensive intestinal adhesions are unrecognized or form subsequent to operation and cause obstruction. The advantages of the vertical abdominal incision in the median line are: (1) A thorough inspection of the pelvic contents is afforded, and it is capable of being extended to permit inspection and palpation of the abdominal viscera. (2) The various complications found may the more readily be promptly treated. Of the disadvantages Montgomery mentions, dependent drainage is not applicable, and there is danger of infection of the abdominal wound with subsequent hernia and a disfiguring cicatrix. The advantages of the Pfannenstiel incision are: (1) It permits a larger exposure of the field for a comparatively small incision. (2) The probability of subsequent hernia is lessened, as the interior and middle lines of closing sutures are at right angles to each other. (3) The incision through the skin is subsequently hidden by the regrowth of the pubic hair. The disadvantages of it are: (1) Its limited application, being too small for removal of large tumors and exploration of the abdominal contents. (2) The necessarily large opening of the cellular tissue renders possible extension of infection to the wound in cases of pelvic pus accumulations.

OPHTHALMOLOGY.

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The Effect of Sclerectomy upon the Circulation of the Eye.—Sclerectomy has hitherto been regarded as favoring the excretion of the intra-ocular fluid solely by the creation of a filtering cicatrix or fistula. BETTREMIEUX (*Clin. optal.*, December 10, 1908, 370) suggests that the ablation of a superficial layer of the sclera brings the deeper vessels of that structure into relation with the vascular network of the conjunctiva

and the subconjunctival tissue; anastomoses result and a collateral circulation is established which favors the outflow of fluid from the interior of the eye. Upon this view sclerectomy is held to be analogous to the creation of adhesions between the epiploön and the abdominal wall to improve the circulation in cirrhosis of the liver.

Mikulicz's Disease.—In RANDOLPH'S case (*Ophth. Record*, January, 1909, 19) there was enormous symmetrical enlargement of the lacrymal glands, compelling the patient to throw the head back so as to see between the narrowed palpebral aperture. The enlargement entirely disappeared after three months, during which a course of potassium iodide had been administered. The parotids began to enlarge after the swelling of the lacrymal glands had disappeared; the right parotid reached the size of a hen's egg; the left was about one-half as large.

Cortical Motor Centres of the Ocular Muscles.—From experiments upon apes, LEVINSOHN (*Ann. d'ocul.*, September, 1908, 217) comes to the following conclusions: Central motor innervation is very important in the ape; it has its seat in the posterior half of the frontal lobe, the angular gyrus, and the occipital lobe. The region anterior to the pre-Rolandic fissure is the most excitable, the occipital lobe next, and the angular gyrus least. Each of these regions is capable of stimulation by itself. Stimulation of the cortex causes primarily contraction of the muscles excited; inhibition of the antagonists is secondary. Extirpation of the cortical zones is almost entirely negative; rapidly disappearing conjugate deviation occurs; the function of lateral movement is preserved.

Peripheral Iridectomy in Glaucoma.—To maintain the action of the sphincter and prevent prolapse of the pillars of the coloboma into the wound, Wöllflin (*Klin. Monatsbl. f. Augenhk.*, November to December, 1908, 534) has proposed and practised in three cases, with satisfactory results, what he terms peripheral iridectomy; that is, excision of a piece of the iris between the sphincter and the periphery, leaving the margin of the pupil intact. The operation is more difficult to perform than ordinary iridectomy, and will occasionally require general narcosis.

Normal Range of Accommodation at Various Ages.—DUANE and THOMAS' determinations (*Trans. Amer. Ophthal. Soc.*, vol. xi, Part III) differ somewhat from those of Donders; the accommodation in childhood and youth was lower—rarely above 14 D. between eight and thirteen. The range does not seem to diminish much between ten and fifteen years. The maximum may even occur at sixteen or eighteen, although this requires further investigation. The accommodation does not decrease steadily at all ages, but appears to remain about stationary for some years and then diminish rapidly; from twenty-five to thirty and again from thirty-five to forty are periods of special stasis, but further observation is necessary; but an abrupt plunge seems to occur at forty and continue until fifty-one, after which age the accommodation remains nearly constant, diminishing not more than 0.5 in ten years. Certain peculiarities in the behavior of the function were found in individual cases, and unequal power in the two eyes was not very uncommon.

Toxic Symptoms following the Instillation of Homatropine Hydrobromate.—In LE FEVRE'S case (*Ophth. Record*, June, 1908, 283) three instillations, 1 grain to 48 minims, in two hours and a half was followed half an hour later by light headedness and faucial dryness. Thickness of the voice and delirium, with hallucinations of the sight and apparently hearing, were present. There was pronounced muscular prostration and incoördination. Recovery was complete in six hours.

Suppuration in the Right Temporal Region.—GAVIN (*Ophth. Record*, May, 1908, 245) reports that a successful operation for abscess in this region was performed, followed two weeks later by left exophthalmos and suppuration from the left nostril. Incisions between the globe and lower lid failed to find the pus; tapping the antrum was also negative. Acute suppuration of the middle ear next developed, which was relieved but not cured by incising the drum. Complete cure followed a radical mastoid operation.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Difference Between the Typhoid Bacillus in the Animal Body and when Grown on Artificial Media.—The decrease in virulence of bacteria when grown on artificial media is a well-established fact, and morphological differences of the same organism under these different conditions of growth have been described. TSUDA (*Zentrabl. f. Bakt.*, 1908, xlviii, 277) has found that typhoid bacilli when grown in blood serum differ from bacilli grown in artificial media in the same way as the bacilli grown in the animal body do. These differences are both morphological and biological. The bacilli grown on serum and those grown in the animal body have the same strong resistance against the agglutinative and bacteriolytic action of immune serum, but neither has increased resistance to phagocytosis. The author believes that this change probably depends upon the difficulty with which the organisms are united with the amboceptors of the immune serum, and is produced by a property of the blood serum which is not to be identified with the bacteriolytic component.

The Etiology and Pathology of Tetany.—RUDINGER (*Ztschr. f. exp. Path. u. Ther.*, 1908, v, 205) presents a discussion of the literature and of his own experiments in order to advance his belief that all forms of tetany are dependent upon an insufficiency of the parathyroid bodies.

He considers that the principal function of the parathyroid bodies is the neuralization of toxic substances that act upon the nervous system, and when this neutralization is not complete there is either outspoken tetany or a tendency to this symptom complex. When a tendency to tetany is present, the phenomenon may be called forth by a number of conditions which do not so effect normal individuals. This belief is substantiated by a series of experiments on cats, in which, after treatment with various poisons (calomel, morphine, atropine, tuberculin, ergotin, and ether), without producing any change in electrical reaction or other disturbances, both the outer parathyroid bodies were removed. The animals were then observed for fourteen days, during which time some did and some did not develop tetany. Those which did not develop tetany were found to have increased electrical excitability and other signs which indicated that a tendency toward tetany was present. In animals that during the first day's observation showed no tetanic convulsions the electrical excitability was increased, and somewhat indefinite tetany was produced by treatment with the poisons that formerly were inert. The author thinks that the tetany of gastro-intestinal origin is produced by toxins formed in the digestive organs which act upon the organism poorly protected, on account of parathyroid insufficiency, against these intestinal toxins. This idea is held in spite of the fact that normal parathyroid bodies have been observed several times in patients dying with this form of tetany. Rudinger emphasizes two lesions of the parathyroids as being especially frequent causes of their insufficiency—hemorrhage into the parathyroid bodies, which he believes is an important lesion in the tetany of childhood, and tuberculosis of the parathyroids. A number of instances of tuberculosis of these bodies have been reported, and the existence of this lesion may be the cause of the frequency of Chvostek's sign in tuberculous patients. Schlesinger noted this sign 64 times in 133 patients. With a parathyroid insufficiency already established, the symptom complex of tetany may be called forth by many different agencies or conditions. Thus, in spite of the diverse forms of the disease, the symptom-complex may be etiologically and pathologically an entity, with various secondary or determining causes.

Enzymes of Tuberculous Tissue.—Opie (*Jour. Exper. Med.*, 1908, x, 645), in several previous papers, has shown that the cells of inflammatory exudates contain enzymes which are capable of digesting proteid material. Two types of enzymes were found to be present: one, leukoprotease, which resided in the polymorphonuclear leukocytes and acted in a neutral or alkaline medium; another, lymphoprotease, a ferment peculiar to the large phagocytic cell or macrophage, and active only in an acid medium. Opie and Borker have now devoted their attention to the study of the cells in tuberculous tissue, and find here again that the tuberculous tissue, like the inflammatory exudates, contains the same types of enzymes. Leukoprotease, the ferment which digests in neutral and alkaline media, is present only during the early stages of the process, and its presence and early disappearance is in direct relation to the invasion of the tissue by polymorphonuclear leukocytes. The amount of lymphoprotease, the enzymes which digest in acid medium, increases during the early stages of the tuberculous process, and in this respect

corresponds closely to the invasion and proliferation of the large epithelioid cell, the cell which evidently contains this enzyme. Its activity is greatest just before caseation takes place, and with the advance of caseation its activity diminishes until, when caseation is far advanced, enzymes are almost totally absent. The authors think it not impossible that caseation which, like autolysis, is accompanied by disappearance of nuclei is in part dependent upon the presence in the cells of the active proteolytic enzyme for a time held in check. Injury to cells by products of the tubercle bacillus or partial anemia, and the results of imperfect vascularization of the tuberculous tissue, may have a part in rendering these cells susceptible to self-digestion. A study of the serum from tuberculous pleural exudates results in rather unexpected findings. Under ordinary circumstances the blood serum, in rather small quantities inhibits completely the action of the leukocytic enzymes. The serum from tuberculous pleural exudates, on the contrary, though during the early stages of the exudation it inhibited the action of the enzymes contained in the large phagocytic cells of the lymph glands, soon lost almost completely this power and itself developed very soon active proteolytic properties. The ability to cause proteolysis increased with the age of exudates. Digestion proceeded best with a neutral reaction. At the same time, the blood serum did not show any diminution in its proteolytic properties. The serum from sterile inflammatory pleural exudates differed from that of the tuberculous exudates in that it inhibited the enzymotic action of leukocytes and showed very little if any power to cause proteolysis.

The Results of Local Tuberculin Reactions.—WOLFF-EISNER and BRANDENSTEIN (*Mitt. aus den Grenz. der Med. u. Chir.*, 1908, xix, 381) discuss the results obtained in the two methods of local application of the tuberculin reaction, namely, the conjunctival and the cutaneous (Piquet) reactions. Their material was composed of surgical cases, especially children. Two facts have been brought out against the value of the conjunctival reaction, its uncertainty and its danger to the eyes. Lately, however, the statistics of Dujour show that the danger to the eyes is very slight, and in over 3000 cases Wolff-Eisner and Brandenstein report but three cases showing inflammatory complications. This fact, they believe, indicates that the danger is very slight when the application of tuberculin is properly performed. They have used the reaction in children with tuberculous lymph glands, in which it was formerly considered particularly dangerous, and had but one ill effect, a mild inflammation lasting but fourteen days. The results of the two methods indicate that the conjunctival reaction, when positive, signifies an active tuberculous process, while the cutaneous reaction is positive when a latent lesion as well as an active one is present. In 1500 clinically non-tuberculous medical cases, Stadelmann and Wolff-Eisner found the conjunctival reaction positive in 15 per cent. and the cutaneous reaction positive in 50 per cent. The cutaneous reaction was positive in 75 per cent. of a series of twenty doctors and nurses working with tuberculous patients. The authors advise the use of a weak solution (1 per cent. of tuberculin, Reute-Enock) for the conjunctival reaction, and believe that the two local reactions should be employed together. The diagnostic and prognostic conclusions to be drawn from such use

have proved useful in surgical as well as in medical practice. In tuberculosis of the lymph glands the conjunctival reaction responded only in cases of acute active tuberculosis, and was negative in the chronic or torpid forms in which the cutaneous reaction was positive. The authors reported few failures with either method, but when deductions are properly drawn from the results the local application of tuberculin can be considered a very valuable procedure for diagnosis.

The Coagulation Time of the Blood and Thrombosis in Phlebitis.—HARLOW BROOKS and CROWELL (*Jour. Exper. Med.*, 1908, ii, 271) have carried on experiments with a view of determining what part an artificially increased or decreased coagulability of the blood plays in the production of thrombosis. They used rabbits, and found that they could decrease the coagulation time of the blood one-half by the daily administration of 2 grams of calcium lactate. On the other hand, they found that they were able to increase the coagulation time one-third by the exhibition of 2 grams of citric acid each day. They further found that the maximum effect of these drugs occurs in two hours after their administration, and probably passes off in twelve hours. To induce thrombosis they injured the vessel walls either by means of clamps or by injections of chemical substances or bacterial cultures into the vein or into its surrounding tissues. They concluded from their experiments that mere stagnation of venous blood produced no marked tendency to thrombosis. In their experiments thrombosis was most readily induced when inflammatory lesions existed in the bloodvessels. They think that purely mechanical lesions do not cause thrombosis except at the immediate point of injury to the vessel wall. Marked artificial increase or decrease of the coagulation time of the blood by the use of calcium lactate or citric acid did not render animals more subject to thrombosis incited by changes other than inflammatory. When true phlebitis existed thrombosis was apt to be more extensive, and less readily absorbed when the coagulation time of the blood was shortened by the use of calcium lactate. It was less extensive and more readily absorbed when the coagulation time was increased by the administration of citric acid.

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